2006

Animal protocol reviews in the United States and Taiwan

Hsin-Yi Yao
San Jose State University

ANIMAL PROTOCOL REVIEWS IN THE UNITED STATES AND TAIWAN

A Thesis

Presented to

The Faculty of the Department of Environmental Studies

San José State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

By

Hsin-Yi Yao

December 2006

INFORMATION TO USERS

The quality of this reproduction is dependent upon the quality of the copy submitted. Broken or indistinct print, colored or poor quality illustrations and photographs, print bleed-through, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

ProQuest Information and Learning Company
300 North Zeeb Road
P.O. Box 1346
Ann Arbor, MI 48106-1346

APPROVED FOR THE DEPARTMENT OF ENVIRONMENTAL STUDIES

Dr. Lynne Trulio, Co-Chair,
Professor, Department of Environmental Studies

Dr. Katherine Kao Cushing, Co-Chair,
Assistant Professor, Department of Environmental Studies

Mr. Larry Young,
Operations Manager, Animal Care Facility

APPROVED FOR THE UNIVERSITY

12/06/06

ABSTRACT

ANIMAL PROTOCOL REVIEWS IN THE UNITED STATES AND TAIWAN

by Hsin-Yi Yao

The United States and Taiwan utilize similar systems to govern the welfare of laboratory animals in that each institution using animals must establish a committee supervising their care and use. Investigators conducting animal experiments must submit a protocol to the committee for approval before initiating the experiments. In the United States, the committee is known as the Institutional Animal Care and Use Committee (IACUC), and in Taiwan it is called the Management Group of Animal Experiments (MGAE). This study uses qualitative interviews and document reviews to compare protocol reviews of IACUCs with those of MGAEs and analyze how regulations and cultural differences affect committee members' review standards and the systems' effectiveness in governing the use of animals in research. This study reveals that regulations have a crucial influence on the protocol reviews of IACUCs and MGAEs. Differences in American and Taiwanese cultures also affect the implementation of regulations and the protocol review systems' effectiveness in protecting animals.

ACKNOWLEDGEMENTS

This research could not be done without the help and support of a number of people. I would like to deeply thank my committee members, Lynne Trulio, Katherine Cushing, and Larry Young, for shepherding me through this long and difficult process. I would also like to express my sincere gratitude to Wu Hung, the President of the Environment & Animal Society of Taiwan (EAST), for guiding me through laboratory animal welfare issues, and Dr. San-Chi Liang, the President of the Chinese Society of Laboratory Animal Sciences, for facilitating my interviews in Taiwan. His generous support was instrumental for conducting this comparative research between the United States and Taiwan. I am also grateful to Dr. Chou-Chu Hong, Dr. Wei-Jeng Chang, Han Chiang, and Ms. Meilyne Chen of the Council of Agriculture for providing me with useful information about Taiwan's care and use of laboratory animals. And I am truly thankful to all my interviewees for their time and sharing.

I would like to thank my many friends, both in Taiwan and in San José, for their support and encouragement in this journey. Without their nagging me, it would have taken even longer to complete this thesis. I would like to acknowledge Davinna Ohlson for proofreading my thesis and providing me with lots of guidance on data analysis and thesis writing. I also appreciate my cousin Chih-Wei Li's sharing of his experience in conducting qualitative research. And special thanks to Professors Wenshu Lee and Phil Wander for caring about me, teaching me how to do thesis defense, and giving me confidence.

I could not have done this without the support of my parents, my aunt and her boyfriend Jim Hoffman, and my boyfriend Chi-Chang Tsai. My parents have always been very caring of me and supportive of my research, even though they knew that their daughter may not earn lots of money from specializing in laboratory animal welfare. My aunt, Yulan Carr, took the best care of me, like a second mother, during these years living together. Many thanks to Jim for spending lots of time and effort in editing and proofreading my thesis as well as other homework. And finally, I would like to thank my boyfriend, Chi-Chang Tsai, for supporting me and waiting for me in Taiwan through all these tough years.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

It is estimated that more than forty-one million laboratory animals worldwide are used each year in teaching, product testing, and various areas of research (Orlans 1998). The United States uses fourteen million of them, which accounts for 34% of the estimate, and makes the country the largest user of laboratory animals in the world (Reinhardt and Reinhardt 2002). Taiwan uses approximately one million animals in laboratories, which is equal to 2% of the figure. The United States and Taiwan utilize similar systems to protect the welfare of these laboratory animals in that investigators conducting activities involving the use of animals must submit protocols to a committee for approval before launching the activities. This thesis compares the implementation of the protocol review systems in the United States and Taiwan, and analyzes their effectiveness in protecting the welfare of animals.

In 1966, the Unites States passed the Animal Welfare Act (AWA), which became its primary law governing the humane treatment of animals, including the transportation, purchase, sale, housing, care, handling, and treatment of warm-blooded animals used for research purposes, exhibition purposes, or as pets, such as dogs, cats, nonhuman primates, and marine mammals. However, birds, rats of the genus *Rattus*, and mice of the genus *Mus* bred for research purposes are currently excluded. Since birds, rats, mice, and cold-blooded animals comprise 90% of all laboratory animals, only 10% of laboratory animals are protected (Reinhardt and Reinhardt 2002).

In 1985, the Food Security Act, an amendment to the Animal Welfare Act, greatly expanded the provisions of the AWA. It requires that all research facilities conducting

animal experiments establish an Institutional Animal Care and Use Committee (IACUC) to supervise the humane treatment of laboratory animals. An IACUC consists of at least three members: a chairman, a veterinarian, and a nonaffiliated member. The attending veterinarian must have received sufficient training and experience in laboratory animal science, and is required to provide adequate veterinary care to the animals at the research facility. The nonaffiliated member represents the general public's concern for humane animal treatment. This person, or any of his or her immediate family members, cannot be affiliated with the research facility (AWA 2002).

The IACUCs are responsible for supervising the welfare of covered species maintained and used in research institutions. Research protocols involving the use of animals must be reviewed for all procedural and ethical issues related to animal welfare, such as the selections of species, the numbers of animals, and the degree of pain and distress animals will undergo (Zerlo, Rudacille, and Goldberg 1994). The committees can withhold approval, require modifications to secure approval on proposed projects, and grant approval on an annual basis for ongoing projects. At least once every six months, IACUCs must evaluate all animal programs and inspect all animal facilities for compliance with regulations. They submit inspection reports to the CEOs of both the Animal Care Program and the research facilities, and recommend any necessary corrective actions. The IACUCs are also responsible for reviewing and investigating concerns of staff and the public about the care and use of animals (AWA 2002).

The Animal Welfare Act sets the baseline standard protecting laboratory animals, although institutions may have to adhere to stricter standards such as the Public Health

Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) which was developed by the Public Health Service (PHS) in 1986. Every PHS agency, and all institutions receiving their financial support, must comply with this policy and follow the *Guide for the Care and Use of Laboratory Animals* (NRC 1996), which is regarded as the major standard in the care and use of laboratory animals in the United States. The *Guide* covers all vertebrate animals used in research, testing, and teaching.

By fiscal year 2004, 1,079 IACUCs had been established under the supervision of USDA (USDA 2004). This number does not include facilities that use only birds, rats, and mice, which are excluded from the protection coverage of the AWA. Approximately 1.1 million animals, not including birds, rats, and mice, were used in 2004 in the United States. The use of birds, rats, and mice brings the total to the fourteen million laboratory animals that are used annually in the United States (Reinhardt and Reinhardt 2002).

In Taiwan, regulations governing the care and use of laboratory animals have been adapted from those used in the United States. In 1998, Taiwan passed the Animal Protection Act (APA) covering vertebrate animals that are fed or kept by humans, including farm animals, laboratory animals, companion animals and other animals. The APA, which is implemented by the Council of Agriculture (COA), directs that the number of animals used in scientific research be reduced to a minimum and that all research be conducted in a way that causes the least pain and suffering to animals. The Experimental Animal Ethics Committee (EAEC), established by the COA, develops regulations and supervises the care and use of laboratory animals. The EAEC typically consists of eleven to fifteen members who are recognized as experts and scholars selected

from related agencies, including at least one veterinarian and one representative from an animal welfare organization (APA 2004).

As in the United States, each institution in Taiwan involved in the care and use of laboratory animals has to set up a Management Group of Animal Experiments (MGAE). It consists of three to fifteen members, including veterinarians or personnel who have received training in laboratory animal management. MGAEs are responsible for reviewing research protocols involving laboratory animals, supervising animal purchasing sources, animal care programs, and the use of animals, and preparing annual review reports on animal research. They are also authorized to discontinue the use of animals when research violates regulations and investigators fail to make corrections within a certain period of time (APA 2004). *A Guidebook for the Care and Use of Laboratory Animals*, published by the Chinese Society of Laboratory Animal Sciences (2001), is the primary reference for all institutions doing animal research.

The establishment of MGAEs in research institutions was enforced by the COA in 2001. By 2003, 190 MGAEs had been founded. In 2002, one million laboratory animals were used in Taiwan, with rodents accounting for approximately 73% of them (COA 2004).

Although the care and use of laboratory animals in Taiwan has been regulated for eight years, the effectiveness of the MGAE system has not yet been examined. The animal protection movement in Taiwan has focused mainly on issues of stray dogs and cats; the public is still unaware of issues concerning the welfare of laboratory animals, farm animals, or other animals utilized by humans. In addition to limited public

information, minimal research currently exists on how well the MGAE system oversees activities involving the use of animals.

For the past twenty years in the United States, the IACUC system's effectiveness has been the subject of serious academic research and discussion. For instance, Dresser (1989) and Plous and Herzog (2001) studied the protocol reviews of IACUCs and found that review standards vary among and within committees. Gluck and Orlans (1997) and Ingham et al. (2000) discussed effective approaches to improve IACUCs' supervision in animal care and use, such as including a diverse membership, and providing training programs for investigators.

Taiwan's MGAE system is similar to the U.S. IACUC system. This thesis compares protocol reviews of MGAEs with those of IACUCs, and analyzes how regulations and cultural differences affect committee members' review standards and the systems' effectiveness in governing the use of animals in research.

Because academic institutions use great numbers of animals in teaching and research and are more open to academic research, my thesis focuses on IACUCs and MGAEs in universities. Two qualitative research methods were employed to address the research objective. One involved interviews with IACUC and MGAE members to compare their review standards and perspectives towards animal use and the review systems' effectiveness. They were also asked to evaluate two hypothetical protocols. The other method involved a thorough comparison of the two countries' laboratory animal protective regulations.

By illustrating the two countries' similarities and differences in review processes and standards, this thesis is intended to help the governments, IACUCs, and MGAEs understand their protocol review systems' effectiveness in protecting animals. It provides recommendations designed to improve the welfare of laboratory animals in the United States and Taiwan. It is also intended to aid the United States to better understand Chinese attitudes toward animals under their cultural and social structures, and thus facilitate better communication between IACUCs and Chinese principle investigators conducting research in the United States.

LITERATURE REVIEW

The Concepts of Animal Rights and Animal Welfare

Early animal rights movements started in the late 18th and early 19th centuries in England and Europe and focused mainly on vivisection. More recently in the 1970s and the 1980s, Peter Singer and Tom Regan introduced animal welfare issues into academic discussions, which brought about the animal rights movements in earnest not only to Europe but throughout the United States as well. Regan argues that humans and animals all possess equal inherent value and the right to be treated with respect; therefore, any kind of human utilization of animals, including animal agriculture, animal experimentation, and commercial and sport hunting, are all fundamentally wrong and should be abolished (Regan 1985). Singer employs utilitarianism, which gives humans and animals equal consideration of interests (Singer 1990). He argues that, although there are important differences between humans and animals that result in their different rights, all are sentient beings that can feel suffering and enjoyment. This capacity for feeling allows humans and animals to receive equal consideration of their interests. According to Singer, "The interests of every being affected by an action are to be taken into account and given the same weight as the like interests of any other being" (Singer 1990, 5). Utilitarianism allows people to utilize animals if the overall benefits of the utilization outweigh the harm it causes to animals. On the other hand, if animal suffering outweighs the benefits of the utilization, the action should not be carried out.

Many countries have passed laws and regulations governing the care and use of laboratory animals based on the concept of "animal welfare," which is an application of

utilitarianism. This point of view is the fundamental philosophy of regulations governing the use of animals in research. For example, in the United Kingdom, cost-benefit analysis is the main criteria to review proposed experiments (Birke and Michael 1996).

The "Three R's" Principle

The "Three R's"—reduction, refinement, and replacement of laboratory animal use—are considered the middle ground for science and animal welfare and are the basic principles for regulations in many countries. The Three R's principle was first introduced by two British scientists, William M.S. Russell and Rex Burch, in 1959. Reduction means using fewer animals to obtain the same amount of data, or obtaining more information from a given number of animals (Zurlo and Goldberg 1998). Refinement is concerned not only with minimizing the pain and suffering of animals during experiments, but also with enhancing their comfort and well-being in daily care (Russell 2002). Refinement methods include the use of pain-relieving drugs, proper handling techniques, environmental enrichment (such as the placement of toys) and group housing for social species. Replacement requires replacing live animals with other methods, such as testing on organisms with limited sentience, testing in vitro systems, and using computer models whenever possible (Zurlo and Goldberg 1998).

Cultural Differences and Attitudes toward Animals

In Western societies, Christianity plays an important role in shaping human relationships with nature. According to Linzey (1998), traditional Christianity has promoted three tendencies that have influenced our attitudes toward animals. First, instrumentalism holds that God created animals for the purpose of serving man's needs.

Second, the concept of "humanocentricity," or anthropocentrism, claims that animals have no ability to rationalize and have no soul; thus, they have no moral status, and humans have no direct duties to them. The third tendency is dualism, which distinguishes between humans and animals based on their ability of rationality. Animals are perceived to have no rational intellect; therefore, they are again considered to have no moral status (Linzey 1998).

However, one can also apply a broader and deeper analysis of Christianity in support of the animal rights movements. By Christian standards, God is the owner of the earth, and humans are only the stewards. This ethic of stewardship requires people to take care of the earth and all living beings. The idea of God's covenant with all living beings, introduced in Genesis 9 of the Old Testament, also supports a close relationship between humans and animals. Therefore, acts of cruelty are morally ungenerous and unacceptable to Christianity (Linzey 1998).

Influenced by Buddhism, Confucianism, and Taoism, the Chinese hold very different perceptions and attitudes toward animals as compared to people of Western societies. Buddhism does not advocate the ethic of stewardship; humans are not superior to animals and do not have control over them. However, a general misunderstanding of reincarnation in Buddhism makes it difficult to promote the animal rights movements in Taiwan. Believing in reincarnation, many people incorrectly consider animals to be inferior to human beings because people who act wrongly will be reborn as animals to a life of suffering. Therefore, animals are viewed as paying for their past sins as humans, and people should not be involved in their rescue (Shih 2005).

Confucianism distinguishes animals from humans in that animals do not possess virtues, such as reverence for parents. Animals are viewed as resources that sustain humans' lives and as gifts sacrificed in ceremonies for gods or ancestors (Blakeley 2003). In Confucianism, the importance of ceremonies and customs outweighs the suffering of animals. Taoism tends to view animals in an aesthetic perspective and values their existence in nature. For example, Chuang Tzu appreciated the freedom and happiness of fish. In his ideal world, humans live with animals harmoniously and peacefully (Wong 1979). Animals are also commonly used in stories to teach people how to act wisely and righteously.

According to Yeh (1995), China's unstable social, natural, and political conditions led the Chinese to hold an indifferent attitude toward animal suffering. Throughout their history, Chinese have struggled to survive and were not concerned about animal welfare. Influenced by Buddhism, they are often unwilling to kill animals with their hands; however, animals that are in conflict with human interests or are destined to die, such as stray dogs or farm animals, are of no concern, and no interest is taken in their demise (Yeh 1995). Lee (2003) argues that there are no considerations about animal protection or about animals in general in the Chinese culture. Even though animals are sometimes deified in Chinese mythology, in general, animals are considered lower than humans and are used as tools or food. Lee (2003) also argues that because the Chinese hold very different perceptions toward animals than those of Western people, it is very difficult for the Chinese to understand and accept the contemporary animal rights movements of Western countries. The concept that humans are the highest form of life

and the Chinese tradition of consuming animals for medicinal purposes also make the animal rights movements unpopular (Shih 2003).

Scholars have discussed the general relationship between Chinese culture and Chinese attitudes toward animals in a broad picture; however, views of people who are involved with animal research have not been studied. This issue is addressed later in this thesis, primarily the Animal Welfare Attitudes section.

IACUCs' Protocol Reviews

The responsibility of IACUCs is to ensure the welfare of laboratory animals. The *Institutional Animal Care and Use Committee Guidebook* (USDHHS 2002a) provides general guidelines for IACUCs in reviewing research protocols, such as methods to ensure minimum numbers of animals are used. However, IACUCs may still possess different criteria when reviewing research protocols. According to Prentice, Crouse, and Ring (1990), institutional values, institutional pressures, prevailing community standards, and pressure from animal protection groups can play an important role in IACUCs' judgments. Other factors, such as committee composition, meeting attendance, length of the meeting, number and complexity of protocols, and order of protocol reviews may also influence their decisions regarding the acceptability of research protocols (Prentice, Crouse, and Ring 1990).

Studies have shown that the IACUCs' criteria for reviewing research protocols vary among and within the IACUCs. Dresser (1989) conducted a survey involving IACUCs that belong to institutions funded by and, thus, subject to the PHS policy. Fifty IACUCs were asked to review four hypothetical research protocols. Their individual

decisions and comments were collected and analyzed. Prior to the publication of the *Institutional Animal Care and Use Committee Guidebook* (USDHHS 2002a), when no guidelines existed for protocol reviews, Dresser (1989) found that standards protecting animals were being developed in the IACUC community; however, the evaluation of scientific merit of a protocol remained problematic. When governments or large nonprofit organizations funded a research project, IACUCs relied on the required peer review to assess its scientific merit. However, when private or small institutions funded projects, IACUCs could only evaluate the scientific merit by their own standards, resulting in inconsistent reviewing results (Dresser 1989).

Plous and Herzog (2001) examined the reliability of IACUCs in their protocol review process. Research protocols previously reviewed by IACUCs were gathered from selected U.S. universities and colleges and then redistributed to the participating IACUCs to be evaluated for a second time. Each IACUC member was asked to provide recommendations about the protocols (i.e., approve as written, contingent approval, defer decision, or disapprove protocol). The members also rated the protocols on several criteria, including the quality of research design, clarity of the research proposal, justification for type and number of animals, scientific value, pain scale classification, and clinical and applied value. After completing their individual reviews, the members were asked to convene at regular IACUC meetings to review the protocols again, following their standard procedures. The study's results indicated that the second committees' reviews were more critical than the original committees' reviews of the protocols (Plous and Herzog 2001). It also indicated that the absence of detailed

classification criteria resulted in a low degree of inter-committee agreement (Plous and Herzog 2001).

These studies demonstrate that the lack of concrete and specific reviewing criteria remain problematic to the review process. Federal regulations require IACUCs to carefully assess and compare the scientific value of research with the pain and suffering it will cause to the animals; however, the evaluation of scientific value is the most controversial aspect of the protocol review process (Prentice, Crouse, and Ring 1990).

In order to understand the process of animal ethical evaluation in Canada, Houde, Dumas, and Leroux (2003) conducted observational studies with three Canadian IACUCs, attending regular IACUC meetings for one year. Individual comments regarding protocols were collected and coded as several categories: scientific, technical, political, human analog, replacement, reduction, and refinement. Their results revealed that technical comments, including conversations about governmental guidelines, operating procedures, degree of invasiveness to animals, personnel qualification, and the final decision to a protocol, were the most frequent and accounted for 41% of all the comments. The replacement, reduction, and refinement categories, also known as the Three R's principle, the foundation of animal ethical evaluation stated in Canadian governmental guidelines, accounted for only 16% of the comments. However, ethical concerns were also expressed in the scientific and technical categories. In addition, the study found that the lay member, representing public concerns of animal use, contributed as many comments as the animal technician or the researcher not using animals. Lay comments were most frequently coded as the Three R's or the technical categories. This

result shows that although the lay member usually has no scientific background, they can actively and beneficially participate in the protocol review process.

The Effectiveness of IACUCs

IACUCs facilitate principal investigators' compliance with animal welfare regulations. Ingham et al. (2000) assessed the quality, efficiency, and effectiveness of an IACUC in facilitating principal investigators to comply with the regulations. A consultant group met with individual IACUC members and gathered opinions concerning their activities along with information involving the committee's interactions with the research community. Through the interviews, twenty-five major principal investigators using animals were identified. The consultant group then collected the investigators' perceptions and opinions of the IACUC's operations, including the protocol review process. Based upon the interviews, the consultant group conducted a written survey that included every category of people working in institutional animal care and research. The survey results showed specific approaches to effective improvement that would meet investigators' expectations. First, the software package used for writing animal protocols was user-unfriendly and should be changed. Second, new investigators should be provided with technical training programs related to the handling and manipulation of animals. Third, a general education program focusing on the rationale and process of protocol reviews should be provided for the entire research community. The survey methodology proved to be very successful in assessing and improving the effectiveness of IACUCs.

Although establishing an oversight committee in every institution using animals for research has become a global trend, Steneck (1997) questioned the creation of IACUCs in the United States. The PHS regulations require an IACUC to consist of at least five members, with only one person needing training or experience in laboratory animal science and medicine, the Doctor of Veterinary Medicine. Thus, he argued that most IACUC members did not have the expertise to work with laboratory animals and, therefore, should not oversee their care and use. He also claimed that one of the problems in establishing IACUCs and more stringent regulations was the shift in resources from research to the burdensome load of paperwork associated with meeting federal regulations. Moreover, IACUCs were given too much authority, which created conflicts of interests. For example, instead of being an independent oversight agency, they had become part of the institution's animal care program, which could result in false reports of institutional compliance. The authority of IACUCs also impacted academic freedom. Steneck (1997) argued that animal care staff, not the IACUCs, should review research protocols; IACUC duties should be limited to setting institutional animal care and use standards, providing guidance regarding ethical issues, and ensuring that regulations are satisfied.

In response to Steneck (1997), Gluck and Orlans (1997) argued that both the welfare of laboratory animals and the understanding between scientific community and the public have been significantly improved as a result of the IACUC system. IACUC members should be willing to learn about laboratory animals and consult other professional groups when necessary. Gluck and Orlans (1997) further suggested that the

size of an IACUC should also be expanded, and diverse members should serve institutional needs. Merely placing the responsibility of reviewing protocols to scientific specialists could lead to fewer adherences to the "Three R's" principle since the pressure of improving animal welfare came primarily from outside the research community. Regarding the IACUCs' impact on academic freedom, Gluck and Orlans (1997) argued that no evidence existed to support the notion that the creation of IACUCs had impeded advances in academic research. Moreover, failure to meet the mental and physical needs of animals is not only cruel but will have an impact on experimental results. Regarding the conflicts of interest, Gluck and Orlans (1997) agreed that so long as the committees are composed of members from within institutions, this issue will continue to exist.

RESEARCH QUESTIONS

The primary research objective of this thesis is to compare the protocol review standards of IACUCs (Institutional Animal Care and Use Committee) with those of MGAEs (Management Group of Animal Experimentation) in American and Taiwanese universities, respectively, and to explore how regulations and cultural differences affect their protocol reviews and the systems' effectiveness in governing animal welfare. Specifically, this thesis addresses the following questions:

1. How do laboratory animal protection regulations in Taiwan differ from those of the United States?
2. How do attitudes toward the use of animals in research differ between IACUC and MGAE members?
3. How do research protocol review standards differ between IACUCs and MGAEs with respect to the Three R's principles of reduction, refinement, and replacement?
4. Are there differences in review procedures, standards, and members' attitudes toward the use of laboratory animals between medical and non-medical schools?
5. How do perceptions of the protocol review systems' effectiveness differ between IACUC and MGAE members?
6. What recommendations can be made to improve the welfare of laboratory animals in the United States and Taiwan?

RESEARCH METHODS

Protocol review systems and standards of university IACUCs and MGAEs were compared to explore how regulations and cultural differences affect these systems and standards. Two public schools in both the United States and Taiwan were selected for the research. I conducted semi-structured, in-person interviews with members on the IACUCs and MGAEs of the selected schools. Laws and regulations governing laboratory animal welfare in the two countries were also compared.

Study Systems

I studied the animal protocol review systems and standards of one public university and one public medical school in each country. To ensure interviewees' confidentiality, the American medical school and university and the Taiwanese medical school and university are referred to as schools A, B, C, and D, respectively. The IACUCs and MGAEs at these schools are similarly referred to as committees A, B, C, and D. Schools A, B, and D were selected because their locations were accessible for me. School C was selected both because of the easy accessibility and because I had known one of its MGAE member.

Medical schools A and C are similar to each other in their use of animals. Both of them have large numbers of new animal protocols each year, with 200 protocols at school A and 180 at school C (Table 1). They also use a variety of species, ranging from small animals such as mice and rats, to large species such as pigs and monkeys.

Universities B and D are quite different from the medical schools regarding the use of animals. Species that they use usually include only rodents, fish, and amphibians

(Table 1). Committee D reviews twenty to thirty new animal protocols each year, and committee B reviews about two to three new protocols annually.

Table 1. Participating universities' uses of laboratory animals.

	United States		Taiwan	
University	**A (Medical School)**	**B (General University)**	**C (Medical School)**	**D (General University)**
Number of new animal protocols per year	200	2-3	180	20-30
Animal species used	Mice, rats, guinea pigs, rabbits, cats, dogs, sheep, pigs, monkeys, finches, fish, frogs, turtles	Mice, frogs	Mice, rats, guinea pigs, hamsters, rabbits, dogs, pigs, monkeys	Mice, rats, rabbits, fish, frog

Due to the large numbers of animal protocols, medical schools A and C both have a large committee consisting of more than ten people, including on-site veterinarians (Table 2). The veterinarian on committee B is not on the university faculty. One veterinarian is in charge of the animal facility at university D, but he has never been on the committee. Committee A has three members who are not affiliated with the school, including one scientist, one private practicing veterinarian, and one nonscientist. Committee B has two nonaffiliated members, including a retired staff member and a scientist. Committees C and D have no nonaffiliated members.

Table 2. Committee compositions. The term "scientist" refers to members, affiliated or not affiliated with the school, who use laboratory animals in teaching or research. Veterinarians are not included, although they also have a scientific background and may use animals as well. The term "nonscientist" refers to members who are not trained to use animals and whose primary interests are not in scientific areas.

Committee	United States		Taiwan	
	A	B	C	D
Total committee members	18	7	15	8
Veterinarian	3	1	2	0
Nonaffiliated member	3	2	0	0
Scientist	13	3	12	7
Nonscientist	1	2	1	1

Study Design and Data Collection

In order to explore preliminary in-depth information about the differences between IACUCs and MGAEs, this research employed qualitative methods, including document reviews and in-person interviews.

Document reviews. The first research question is addressed through a comprehensive document review and analysis. I compared and analyzed current regulations governing the care and use of laboratory animals in the United States and Taiwan. These regulations include the U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (U.S. Government Principles); the federal Animal Welfare Act (AWA) and Animal Welfare Regulations (AWRs); the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy); the *Institutional Animal Care and Use Committee Guidebook* developed by the U.S. Department of Health and Human Services (USDHHS); the Taiwanese Animal Protection Act (APA); and the Regulation for Establishing the Management Group of Animal Experiments (Regulation). Elements of these regulations that were analyzed include the compositions, responsibilities, authorities, protocol review

criteria, and protocol review processes of IACUCs and MGAEs. The document reviews were conducted from September 2005 to April 2006.

Interviews. To address research questions 2, 3, 4, and 5, I conducted semi-structured, in-person interviews with MGAE members at schools C and D in September and October 2005, and with IACUC members at schools A and B in February and March 2006. I recorded these interviews using a digital voice recorder and kept notes when necessary.

In Taiwan, members on committee C were identified through staff of the animal care facility, and members on committee D were found directly on the school website. Each member was contacted individually by e-mail or phone. A total of fourteen committee members, nine on committee C and five on committee D, agreed to be interviewed (Table 3).

In the United States, contact information of IACUC members could not be located from websites of the selected schools. Larry Young, a thesis committee member and the Operations Manager of the Animal Care Facility at San José State University, served as a liaison and connected me with his colleagues, who introduced me to other members and gave me the contact information of people who were willing to participate in the interviews. Eleven members, seven on committee A and four on committee B, were interviewed (Table 3).

Table 3. Interviewed members' membership. Definitions of "scientist" and "nonscientist" are as same as Table 2.

Committee	United States			Taiwan		
	A	B	Total	C	D	Total
Total interviewed members	7	4	11	9	5	14
Veterinarian	2	0	2	2	0	2
Nonaffiliated member	1	2	3	0	0	0
Scientist	4	3	7	6	5	11
Nonscientist	1	1	2	1	0	1

The interviews consisted of four parts: general information, review processes and standards, hypothetical protocol reviews, and personal information and attitudes. The interviews began with general questions about the interviewees, such as their position and service experience on the committee, number of protocols they review annually, and references or guidelines they use when reviewing protocols (Appendix A).

The second set of questions was aimed at understanding interviewees' review processes and standards, and their views about the protocol review systems. Questions included what three aspects of a protocol that they consider most important, their reasons and standards for these aspects, their biggest frustration when reviewing protocols, and their opinions about and recommendations for improving the protocol review system.

In the third part of the interview, interviewees were asked to review two hypothetical animal research protocols in order to collect information about their review methods and standards. The first hypothetical protocol was for an immunological study that explored passive immunity in a parabiotic mouse model, which involved surgical conjoining of two mice. This animal model was selected due to its controversial nature. The protocol was intentionally designed to provide vague or inadequate information about justification for the research, number of animals to be used, research design,

scientific value of the research, and literature search of relevant studies. On the other hand, the protocol provided clear descriptions of sound procedural design and adequate veterinary care.

The second hypothetical protocol was modified from Stafford, Brewer, and Gessaman (2003) and dealt with studying the food selection behavior of captured wild birds. For IACUC interviewees, the bird species used in the protocol was the common starling (*Sturnus vulgaris*), a common, non-native species in the United States. The protocol distributed to MGAE members used white-vented myna (*Acridotheres javanicus*), a common, non-native species in Taiwan. This protocol called for the use of a species in the research study that was very abundant, which allowed for a large sample size of 100 birds. The birds would be confined for ninety days and provided with a variety of foods, including live, frozen, and pesticide-killed invertebrates. At the end of the study, the animals would be euthanized for liver analysis of pesticide content. This protocol was designed to be strong in its rationale, but problematic in the selection of animal model, animal number, and study design.

The format of the hypothetical protocols was only slightly modified from the standard form provided by Taiwan's government. For the United States, the format was shorter and simpler compared to what most institutions use, but it did cover basic elements of an animal care and use proposal, such as research objectives, animal numbers to be used, study designs and procedures, and sacrifice methods for animals at the end of the study.

Interviewees were asked to review these two hypothetical protocols using their standard protocol review method. I first asked for their comments and opinions about the protocols. Then, in order to understand their standards and judgments more thoroughly, I asked them a series of questions, modified from Plous and Herzog (2001), regarding the scientific value of the proposed experiments, the experimental designs and procedures, the types and numbers of animals used, and the amount of pain and distress the animals were expected to endure. These are criteria that federal and professional guidelines require IACUCs to consider when reviewing protocols (Plous and Herzog 2001).

During the last part of the interview, I questioned interviewees about their attitudes toward using animals in research and about their age and life experience, such as living abroad, religion, and experience with pets.

Data Analysis

I transcribed all recorded interviews and wrote up field notes based on observations recorded at the study sites. I analyzed data by performing a line-by-line coding of both interviews and field notes. Through this process, themes of IACUCs and MGAEs were identified independently. A focused coding of the data was then performed to further identify and analyze major themes in the responses of interviewees from each country. Finally, major themes of IACUCs were compared with those of MGAEs, and relationships between the themes, regulations, and cultural differences were analyzed.

Limitations

This research has several limitations. Data was only gathered from individual members outside committee meetings in both countries. Therefore, this research does not

directly record the discussions and interactions among committee members, which are often essential in the decision-making process for approving or rejecting a protocol.

Second, since participants were self-selected, it is possible that only people concerned about animal welfare chose to participate in the research; therefore, the results may indicate the "best case scenario" by reporting only the responses of the most concerned members. Also, some interviewees might have emphasized their concerns about animals and reviewed the hypothetical protocols more carefully than usual since they knew their responses would be analyzed and compared with those of other interviewees. Conversely, interviewees might have devoted less time and effort to the protocols because they were hypothetical and generic.

Finally, IACUCs, formed twenty years ago, might be more experienced in reviewing protocols than the MGAEs, which only began their implementation in 2001 and might still be developing their review standards. Since only two committees in each country were studied, this research also does not reflect conditions nationwide. Rather, it reflects only the review systems of the four participating committees and should be viewed as a case study.

However, this research does provide preliminary information about how IACUC and MGAE members think about animals and review animal protocols and reflects the influences of regulations and cultures on their attitudes and perspectives. My research also explores the effectiveness of the review systems under current regulations and provides recommendations to improve the welfare of laboratory animals.

ANIMAL WELFARE REGULATIONS

Relevance to Research Question

This chapter analyzes laws and regulations governing the welfare of laboratory animals in the United States and Taiwan (Research Question 1). A comparative analysis of current regulations specifically overseeing the welfare of laboratory animals (i.e., composition, responsibilities, authorities, protocol review criteria, and protocol review processes of IACUCs and MGAEs) in these two countries is presented.

Laboratory Animal Welfare Regulations in the United States and Taiwan

In the United States, the AWA and the PHS Policy are the primary regulatory regimes governing laboratory animal welfare. The AWA requires each research facility utilizing covered animal species to establish an Institutional Animal Care and Use Committee (IACUC). Institutions using birds, rats, mice, and cold-blooded species are exempted (AWA 2002). The PHS also requires the IACUC system for institutions receiving its funds, but the requirements are broader than those mandated by the AWA. All vertebrate animal species are covered by the PHS Policy (USDHHS 2002b).

Taiwan requires a Management Group of Animal Experiments (MGAE), whose functions are similar to that of the IACUC, to be formed in institutions performing scientific experiments (APA 2004). The Regulation for Establishing the Management Group of Animal Experiments (Regulation), which is set up by the Council of Agriculture (COA) under the Animal Protection Act, specifies functions and responsibilities of MGAEs. However, the MGAEs' duties were described vaguely in the

Regulation; subsequently, more detailed and specific guidance was developed and promulgated by the COA.

Committee composition. Significant differences regarding committee composition exist as a result of the two countries' regulations (Table 4). In the United States, as required by the AWA, an IACUC must be composed of at least three members, including a Doctor of Veterinary Medicine trained or experienced in laboratory animal science and medicine, and a member who is not affiliated with the research facility in any way. In PHS-funded institutions, the IACUCs must have at least five members, including a veterinarian, a nonaffiliated member, at least one scientist who is experienced in conducting animal research, and at least one member whose interest is not in scientific areas and could provide opinions from a lay or opposite perspective (USDHHS 2002b).

However, in Taiwan, a MGAE does not necessarily have to have a veterinarian member. Either a veterinarian or a person who has passed a training program provided by a government-certified institution fulfills current regulations. In addition, the regulations do not require a nonaffiliated person to serve on the committee. MGAEs are allowed to consist of three to fifteen members, regardless of members' expertise, affiliation, or concerns (APA 2004). Thus, all members serving on an MGAE could potentially be scientists conducting research on animals.

Table 4. Composition requirements of IACUCs and MGAEs.

	U.S. Animal Welfare Act and Regulations	PHS Policy	Taiwan's Animal Protection Act and Regulation
Numbers of committee members	≥ 3	≥ 5	3 to 15
Requirements of Doctor of Veterinary Medicine member	At least one member shall be a Doctor of Veterinary Medicine.	At least one member shall be a Doctor of Veterinary Medicine.	The committee shall have a Doctor of Veterinary Medicine or a person who has passed a training course held by the government or a commissioned training institution.
Requirements of non-affiliated member	At least one member shall not be affiliated with the institution and does not have an immediate family member who is affiliated with the institution.	At least one member shall not be affiliated with the institution and does not have an immediate family member who is affiliated with the institution.	Not specified.
Requirements of scientific member	Not specified.	At least one member shall be a practicing scientist experienced in research involving animals.	Not specified.
Requirements of non-scientific member	Not specified.	At least one member whose primary concerns are in a nonscientific area.	Not specified.
Other requirements	If the committee consists of more than three members, not more than three members shall be from the same administrative unit.		

Data sources: AWA 2002, USDHHS 2002a, 2002b, APA 2004, and COA 2003.

Committee authorities and responsibilities. Overall, IACUCs and MGAEs have similar authorities and responsibilities (Table 5). The AWA and the PHS Policy set identical rules for IACUCs. The committees are required to review research institutions' animal care program as well as all animal facilities at least once every six months. Their evaluations must be documented, submitted to the Institutional Official (IO), and kept by the institutions (AWA 2002 and USDHHS 2002b). MGAEs are also obligated to conduct

this internal inspection once every six months. Committee reports need to be submitted directly to the COA annually and maintained by the institutions for three years (COA 2003).

Table 5. Functions, responsibilities, and authorities of IACUCs and MGAEs.

	U.S. Animal Welfare Act and Regulations	**PHS Policy**	**Taiwan's Animal Protection Act and Regulations**
Frequency of review of animal care and use program	At least once every six months.	At least once every six months.	Every six months.
Inspection of animal facilities	At least once every six months.	At least once every six months.	Every six months.
Frequency of submitting reports of the evaluations of animal program and facilities	Semi-annually to the Institutional Official (IO). The reports must be maintained by the research facility and made available to Animal and Plant Health Inspection Service (APHIS) and funding federal agencies upon request.	Semi-annually to the Institutional Official (IO). The reports must be maintained by the institution and made available to Office of Laboratory Animal Welfare (OLAW) upon request.	Annually to the Council of Agriculture (COA).
Review concerns and noncompliance regarding the care and use of animals	Yes.	Yes.	Not specified.
Make recommendations	Any aspect of the animal program, facilities, or personnel training.	Any aspect of the animal program, facilities, or personnel training.	The institution's animal facilities.
Review proposed activities related to the care and use of animals	Yes.	Yes.	Yes.
Review a proposed change regarding the care and use of animals in ongoing activities	Yes.	Yes.	Not specified.
Authority to suspend an activity	If the activity is not conducted in accordance with the investigator's protocol.	If the activity is not conducted in accordance with the Animal Welfare Act, the *Guide*, the institution's Assurance, or PHS Policy.	If the activity violates the regulations and is not corrected within a certain period of time.

Data Sources: AWA 2002, USDHHS 2002b, APA 2004, and COA 2003.

Both IACUCs and MGAEs make recommendations regarding the institutions' animal care and use (Table 5). IACUCs also investigate concerns and noncompliance involving animals (AWRs 2002 and USDHHS 2002b). While no such component is specified in Taiwan's regulations and guidance, MGAEs can still review and inspect any possible deviations because the Regulation gives them the authority to supervise any actions related to the acquisition, housing, management, and scientific applications of animals (COA 2003).

Deficiencies found in the animal care programs and facilities are taken more seriously in the United States than in Taiwan. In the United States, IACUCs must distinguish major deficiencies from minor deficiencies and develop specific corrective plans and timelines for each one. If a major deficiency is not corrected within the specified schedule, IACUCs must notify the Animal and Plant Health Inspection Service (APHIS) within fifteen days (AWRs 2002 and USDHHS 2002b). Conversely, MGAEs are not required to report deficiencies to the COA (COA 2003). Current COA guidance allows institutions to make corrective actions without notifying the agency, and the development of corrective plans and schedules are not addressed.

The most important function of IACUCs and MGAEs is to make sure that experiments involving animals will be conducted in accordance with all regulations. Proposed experiments must be reviewed and approved for every aspect of animal care and use prior to commencing (Table 5). Once approved, IACUCs and MGAEs still retain oversight over these projects. In the United States, if modifications need to be made to an ongoing project, the law requires the principal investigator to obtain approval from the

IACUC before the changes are instituted (AWRs 2002 and USDHHS 2002b). In Taiwan, legal procedures that investigators and MGAEs should follow when dealing with modifications are not addressed in the regulations. Instead, the regulations call for MGAEs to terminate any experiment that violates regulations if the violation is not corrected within a given time (COA 2003). In other words, investigators are allowed to make corrections before projects are stopped. Conversely, IACUCs are authorized to suspend an experiment immediately when noncompliance is found (AWRs 2002 and USDHHS 2002b). Regulations in Taiwan allow more flexibility to investigators than those in the United States.

Protocol review criteria. To facilitate IACUCs' and investigators' compliance with laws and regulations, protocol review guidelines and criteria are established by the U.S. Government Principles, the AWRs, and the PHS Policy. Taiwan currently lacks equivalent regulatory review criteria. Rather, general guidelines regarding the use of laboratory animals can be found in the APA and the Regulation. This section enumerates guidelines and criteria provided by the above laws and regulations in both countries following the sequence of replacement, reduction, refinement, and personnel qualification.

Replacement refers to the substitution of animals with non-living techniques, such as computer models, or other living beings that are less sentient, such as in-vitro systems, invertebrates, plants, and bacteria. Using other species of animals that are lower on the phylogenetic scale is also viewed as a replacement alternative (USDHHS 2002a). When writing protocols, investigators in the United States must provide their rationale for using

live animals and for the appropriateness of the selected species. Investigators must also describe the benefit and significance of the research to demonstrate its necessity. The U.S. Government Principles require that procedures involving animals be considered for "their scientific relevance to human or animal health, the advancement of knowledge, or the good of society" (USOSTP 1985, Principle II). Investigators should also demonstrate that their studies do not duplicate previous research (AWRs 2003). The U.S. Government Principles and the PHS Policy further require investigators consider replacing animals with non-living systems (USOSTP 1985 and USDHHS 2002b). To fulfill this requirement, IACUCs often ask investigators to conduct a literature search for alternatives to live animals. Unfortunately, criteria for the replacement of animal use have not been addressed in Taiwan's animal laws and regulations.

The reduction principle requires using minimum numbers of animals while being consistent with research design. The APA of Taiwan mandates that "the numbers of animals used in scientific applications shall be reduced to a possible minimum" (APA 2004, Ch. III, Article 15). Specifically, the U.S. AWRs and PHS Policy require that research protocols include a justification of the rationale for the numbers of animals used. IACUCs must be sure that the protocols ask for minimum numbers of animals used while still being able to obtain valid experimental results (AWRs 2002 and USDHHS 2002b).

Several methods exist for reducing animal numbers in experiments. First, proper choice of study groups and statistical analyses help to decide the appropriate number of animals to be used. Second, using inbred strains of animals that are genetically similar can reduce individual variability and, thus, the number of animals needed (USDHHS

2002a). Third, adequate veterinary care that maintains animal health will keep the loss of animals to a minimum. Finally, a pilot study with only a few animals is often recommended for innovative studies to evaluate the proposed procedures and possible results.

Other reduction approaches include maximizing study results with a smaller sample size by employing statistical software to generate the most information from the fewest numbers of animals or by sharing animal tissue with other research projects after an experiment is finished and the animals are euthanized (USDHHS 2002a).

Refinement refers to any approach that reduces unnecessary animal pain, distress, and discomfort. Among the Three R's principle, refinement directly influences animals' well-being and comprises most of the two countries' regulations in protocol review criteria. Taiwan's APA briefly states, "The [scientific] application shall be done in a way that afflicts the least pain or hurt on the animals" (APA 2004, Ch. III, Article 15). In contrast, regulations in the United States provide a much more detailed and complete guidance of refinement approaches. Procedures performed on animals must avoid or minimize pain, distress, and discomfort. U.S. regulations explicitly state that unless pain and distress cannot be relieved due to scientific reasons, investigators must use sedation, analgesia, or anesthesia on animals enduring more than momentary or slight pain or distress (AWRs 2002, USDHHS 2002b, and USOSTP 1985). Investigators also have to conduct a literature search for less painful alternative procedures, such as less invasive imaging techniques instead of open-wound surgeries (USDHHS 2002b).

Moreover, U.S. regulations require that if severe or chronic pain or distress is anticipated to take place, that the animals be painlessly killed, unless there is overriding justification to continue the experiment (AWRs 2002, USDHHS 2002b, and USOSTP 1985). This requirement entails humane endpoints for animal experiments. The U.S. Department of Health and Human Services (USDHHS) defines humane endpoints as "criteria used to end experimental studies earlier in order to avoid or terminate unrelieved pain and/or distress" (USDHHS 2002a, 103). Research protocols should include specific criteria to determine the earliest time at which animals can be painlessly euthanized without interfering with study results.

The concept of humane endpoints is also found in Taiwan's APA. The APA requires that after scientific applications, animals should be checked immediately for quality of life. If animals have lost limbs or organs, or if they are suffering from pain, they must be killed using the least painful method (APA 2004).

The U.S. AWRs set requirements for operative procedures. First, all surgeries and operative procedures on covered species must be conducted using aseptic techniques. Second, a major operative procedure on non-rodent animals must be performed in a dedicated facility designed for that procedure. However, operative procedures of field studies are allowed to be conducted at field sites. Third, no animal should be used in more than one major operative procedure unless a justification, such as for research purposes or for veterinary care, is presented (AWRs 2002). Similarly, Taiwan's APA requires that unless there is a scientific reason, animals should be allowed to fully recover their physical functions before being involved in another scientific application (APA

2004). Nevertheless, animals are not protected from being used in more than one major operative procedure.

Besides relieving pain and distress during experimental procedures, IACUCs need to assess whether the living conditions of proposed animals are appropriate to the species and minimize harm and discomfort. Proper housing and care contributes to animals' overall health and well-being and is an essential component of refinement. Regulations require the care of the animals to be directed by a veterinarian or a scientist trained and experienced in the handling and care of the species (AWRs 2002, USDHHS 2002b, and USOSTP 1985). USDHHS further recommends that IACUCs "consider that environmental factors, such as noises, odors, infrequent or inexperienced handling, or boredom from lack of environmental stimulation can cause unnecessary distress" (USDHHS 2002a, 100).

Among these environmental factors, animal boredom has been one of the most crucial and challenging aspects to resolve. Animals living in a monotonous environment feel bored, frustrated, and distressed (Wemelsfelder 1998). To improve the psychological well-being of animals, environmental enrichment should be implemented in animal housing facilities. The AWRs require that non-human primates must be provided with environmental enrichment (AWRs 2002). However, to ensure the well-being of other animal species, IACUCs should also enhance environmental enrichment whenever possible (USDHHS 2002a).

U.S. regulations require personnel conducting procedures on animals to be well-trained and qualified to perform such manipulations on the particular species of animals

(AWRs 2002, USDHHS 2002b, and USOSTP 1985). An effective way for IACUCs to evaluate personnel qualifications is to include a review checklist of the individual's proficiencies and training in protocol applications (USDHHS 2002a).

Protocol review process. Both the United States and Taiwan allow flexibility in the protocol review process. Research institutions develop their own review procedures within regulatory frameworks.

In Taiwan, regulations or guidance regarding protocol review procedures have not been developed to date. The Regulation for Establishing the Management Group of Animal Experiments states that "people who intend to conduct scientific applications should submit applications for the species, strains, numbers, and experimental designs. The experiments cannot be conducted until being reviewed and approved by the MGAEs" (COA 2003, Article 4). However, no further guidance is provided regarding how this course of action should proceed. Given this complete flexibility, review processes may vary among institutions, according to their needs and limitations.

The AWA and PHS Policy establish criteria for review processes while allowing institutions to develop their own review procedures. IACUCs can conduct either a full committee review or a designated member review. Protocols reviewed by a full committee are evaluated at a committee meeting by quorum of its members. With designated member review, the committee chair may designate one or more members to perform the reviews, although other members can still participate in the process. Each member must be provided with a list of protocol titles and descriptions prior to the review. Members should also be able to obtain the actual protocols and request a full committee

review whenever needed. If a member has a conflict of interest with a particular proposal (e.g., if the member is involved in the project), he or she should not participate in the review process. In those cases in which protocols are too specialized for IACUCs to evaluate, the committees may consult with outside experts to assist the review (AWRs 2002 and USDHHS 2002b).

The protocol reviews will result in one of three outcomes: approval as presented, modifications required to secure approval, and approval withheld. Investigators must be informed by written statements about IACUCs' review decisions and have the opportunity to respond (AWRs 2002 and USDHS 2002b).

IACUCs oversee ongoing projects for their compliance with the approved protocols. The AWRs require an annual review, which is often satisfied by annual reports from investigators (USDHHS 2002a). The PHS Policy requires a complete triennial review, which requires investigators to submit new protocols every three years to be evaluated again (USDHHS 2002b). IACUCs can also suspend an activity that is not being conducted according to protocol. The suspension should be decided in a convened IACUC meeting, and the IO must take corrective actions and report the case to the APHIS, the OLAW, or both agencies (AWRs 2002 and USDHHS 2002b).

ANIMAL WELFARE ATTITUDES

Relevance to Research Question

The attitudes of IACUC and MGAE interviewees toward the use of animals in research reflect cultural differences between the United States and Taiwan. This chapter illustrates how IACUC and MGAE interviewees perceive the utilization of animals in research as well as the human relationship with them and also discusses the role of different cultural backgrounds in shaping their attitudes (Research Question 2).

Do Animals Have Rights?

Significant differences exist between interviewees in Taiwan and in the United States as to whether or not humans have the right to use animals in research. Nearly all IACUC interviewees felt that animal research is ethically correct or acceptable. They believed that animals are not equal to human beings and do not possess the right to be free from manipulation in research. As representative of most IACUC interviewees' opinion, one member on committee A said, "My opinion is that rights belong to people and have [to] do [with] responsibility. I don't ascribe rights to animals. . . . I believe that it's okay to kill animals for food. And I believe it's also necessary to kill animals for medical research or for bio-medical research."[1]

Interviewees in the United States viewed animals to be under humans' custody. This sense of stewardship is derived from the traditional Western culture, in which animals are created by God to serve humans' needs. In this sense, humans have control over animals as well as the responsibility to take care of animals. One interviewee from

university B said, "Because we ourselves, self-determining species, have control over animals, then it's up to us to make sure that the animals don't suffer."[2]

MGAE interviewees, however, demonstrated more diverse, complicated, and sometimes conflicting perspectives regarding this issue, which reflects the Chinese multi-dimensional social and cultural background. Most of the interviewees agreed that humans can use animals in experiments; however, more than half of them also believed animals have rights. "Of course animals have rights. There's no doubt about that."[3]

Several interviewees in Taiwan emphasized that all forms of life should be viewed and respected equally. They believed that animals, plants, and other forms of life are no different because they are all living. To them, animal research is justified since we also use plants and other living organisms for experiments. One interviewee said,

> I basically respect animals' rights to live. All living organisms have rights to live, not only animals but also plants. . . . We should respect every organism which is a life. However, I can't totally agree with the statement that we have no reason to do animal experiments because animals have their rights to live. The reason why I disagree with it is because in that way, we should not use any living being in experiments. In other words, I don't think a life should be distinguished to be higher or lower than another, and if it's okay to use plants in experiments but not okay to use animals, then this is not justifiable to me. If somebody tells me that "You invade the rights of rabbits and mice by doing research on them," then I'll say, "Doing experiment on *E.coli* also invade their rights to live." I think life is life and we shouldn't destroy it. But we destroy or invade others rights to live with a reason. I think an experimenter should not sacrifice a life without a purpose.[4]

Some MGAE members also agreed that all lives are equal, and people are no higher than animals in any way. However, they justified doing animal research by applying Darwin's theory of natural selection. "I agree that animals have their rights to

live. However, I also believe that each species of life on earth needs to compete against each other for existence. . . . The purpose of human being's existence is to pursue the maximum welfare of ourselves. So if an experiment is for this purpose and it needs to use animals, then we have to do it, otherwise humans will not be able to advance."[5]

These interviewees considered the human relationship with laboratory animals to be the same as with wild animals in a natural environment, in that humans and animals all compete for existence. However, a number of MGAE interviewees also distinguished laboratory animals from wild animals. They believed that laboratory animals are bred by humans for research purposes and, thus, ought to be viewed and treated differently from animals living in the wild. Several interviewees mentioned that the purpose of laboratory animals to live their lives is to be used for experimentation. Therefore, "if the experiment is well done, their most important mission since birth is completed."[6]

On the other hand, wild animals are assigned total freedom and full respect. "Things living in nature are not for you to do experiments."[7] The use of man-made laboratory animals is acceptable because "this situation is different from killing animals in natural environment."[8]

Interestingly, one IACUC interviewee who was born in Taiwan and moved to the United States at an early age shared the same perspective as his Taiwanese counterparts. "I do believe animals have the right to live. But also, I am not a vegetarian, and I believe we do raise animals for nutritional purposes. To that extent, I also think that we raise animals to advance our science," he said. "I think [laboratory animals] are different from wild animals, but they are not that much different than domestic animals because they are

all rose [*sic*] for purposes."[9] He was the only interviewee in the United States that distinguished laboratory animals from wild animals when talking about animal rights.

The separation of moral consideration between animals raised for research purposes and animals living in the wild reflects typical Chinese attitudes toward animals. When no conflicts of interests exist, the Chinese look kindly upon animals. An old saying goes, "Love the rats, leave the rice; pity the moths, turn off the lights" (Yeh 1995). Still, Chinese view animals raised for research and other purposes as merely human's tool for life sustenance; in this context, the feelings of animals are often ignored. Indeed, although they were not necessarily careless about animal feelings, the MGAE interviewees believed, without considering the intrinsic value of an animal being as a living creature, that the life mission of laboratory animals is to be experimented on.

While many MGAE interviewees did not feel that animals are inferior to humans, some held the similar belief of IACUC interviewees, namely that humans are superior to animals. One MGAE interviewee said, "We use animals in research for humans' welfare. Therefore, humans are put on a higher position. . . . If you don't use animals, then it is humans that die."[10] Similarly, an IACUC interviewee said, "I think that I'm committed to improving the quality of humans first. And if that means we need to conduct studies on animals, then I'm comfortable doing that in order to improve the quality of humans. I put humans on the top of the list."[11]

Different understandings and interpretations of Buddhism led to conflicting attitudes toward animals between MGAE interviewees. One Buddhist interviewee believed that the killing of animals for research is morally justified because it benefits

human beings. "Of course animals are more inferior. From the standpoint of Buddhism maybe they have done something before, so they become animals through reincarnation. . . . However, they are now creating benefits for humans."[12] The interviewee believed that animals also accumulate benefits for themselves while creating benefits for humans. However, some other MGAE interviewees referred to the Buddhist philosophy that "All lives are equal," and agreed that it is selfish of humans to use animals in research. "Although I'm not a Buddhist, I agree that all lives are equal. . . . However, humans are very selfish. You see, we spend great amounts of effort to live longer, live healthier, and live happier. . . . Humans always think they are wonderful . . . so it's worth using animals in any experiment. This is actually a conflict to me."[13]

Sense of Responsibility

Although interviewees in the two countries have different perspectives regarding the status of animals and their relationship with humans, they all agreed that as long as animals are used in research, the animals must be treated humanely with the pain and distress being reduced to a minimum. "It's very important that we treat them so the animals experience the least amount of pain or distress, not just pain but distress, mental distress."[14] Furthermore, interviewees considered it to be their responsibility to guard the welfare of animals. An MGAE member on committee C said, "Since I have used so many mice, it's my responsibility to make sure that animals receive more protection from the system."[15] An IACUC member on committee A added,

> There are a lot of human studies going on in this university. But every human subject signs a form of consent, so they are choosing to be experimented on. Animals don't have that choice. So that puts a huge burden of responsibility on us to make sure that whatever

> you're going to be doing to the animals is absolutely necessary, and that the welfare of the animals as much as it can be, as possible, is the number one priority, based on the restrictions provided by the necessity of what you have to do to the animals in order to get your research done.[16]

To IACUC interviewees, humans bear a responsibility to care for all animals, including laboratory and wild animals, because humans have stewardship and control over them. It seemed to be so natural for the interviewees to think this way that most of them took it for granted and expressed their attitudes without any explanation: "I think it's always our responsibility to care for animals."[17] The influence of Christianity in forming this attitude of stewardship was illustrated in another interviewee's narration, "Animals are created by God . . . so we have a responsibility to animals to treat them as best we can."[18]

For MGAE interviewees, the sense of responsibility comes not from a perspective of stewardship but rather from a recognition and appreciation of the sacrifice of animals to advance knowledge and improve the human condition. An MGAE interviewee said, "Since they contribute their bodies to us, you should reduce their pain to a minimum. And of course, don't use them if it's not necessary."[19] Another interviewee added, "We thank them for their sacrifice and contributions."[20]

One MGAE interviewee told me his story about looking for ways to substitute killing rabbits at the end of his research. His research required the extraction of antibody from rabbits, but the animals stayed healthy and intact after the experiment. Thus, he tried different ways to save the animals, including releasing them into the wild, finding homes for them, and asking a zoo for acceptance. "Because they have helped me, I truly

didn't want to kill them," he said. "They have made contributions to us. How can we be so hardhearted to kill them?"[21]

An IACUC interviewee also talked about finding homes for her experimental dogs whenever possible. Being concerned about not the contributions of animals but more their nature and relationship with humans, she said, "They were lovely animals. . . . These animals are real pets."[22]

While interviewees in both countries agreed that humankind bears a responsibility to treat laboratory animals humanely, their perspectives were borne of different cultural contexts. American interviewees have a sense of stewardship; they felt that because humans have control over animals, it is their responsibility to care for their well-being. Taiwanese interviewees, on the other hand, believed in reciprocity. They believed that laboratory animals ought to be treated well because they perform a service for humans.

Influence of the Three R's Principle on Animal Welfare Attitudes

Interviewees in both countries spoke not only of the humane treatment but also the replacement and reduction of animals in research, demonstrating that no matter what their attitudes toward using animals in research are, the Three R's principle has been well-recognized as the criteria of using animal subjects. "I think it is important for humans to do research, and it's important to do animal research as part of the overall medical research situation. But it has to be done humanely, without causing undue pain or discomfort to animals."[23] Another interviewee added, "If five animals are enough, don't use fifty."[24]

Interviewees were also critical about whether proposed research is likely to produce good data and contribute to the scientific body of knowledge. One interviewee said, "I think it is very important if we're going to use an animal to better a human condition, but that act has to be justified. . . . I would want to know the act is justified and warranted and likely to produce good data."[25]

IMPLEMENTATION OF PROTOCOL REVIEWS

Relevance to Research Question

Regulations require IACUC and MGAE members to review every item in an animal protocol and determine whether all aspects of the research will be conducted in accordance with regulations and humane standards. In this chapter, I explore the implementation of these regulations by IACUCs and MGAEs. First, I introduce the protocol review processes of each committee. Then, interviewees' review priorities in protocols and their reviews of the hypothetical protocols are discussed and compared. Specifically, their practices of the Three R's principle in protocol reviews are analyzed (Research Question 3).

Protocol Review Processes

Regulations in both countries allow flexibility in the protocol review process, and each committee establishes its own review procedures. In my research, review processes differ among the four committees.

Committee A, which, on average, reviews two hundred protocols per year, utilizes an extensive three-layer review system. After an investigator submits her protocol through an online system, an administrative staff person and a veterinarian conduct a pre-review to make sure that the protocol has been filled out completely and that each procedure meets the highest humane standards. These two pre-reviewers make recommendations on the protocol and send it back to the investigator to address their concerns. The protocol is not reviewed by other committee members until the pre-reviewers are satisfied with its content (Figure 1).

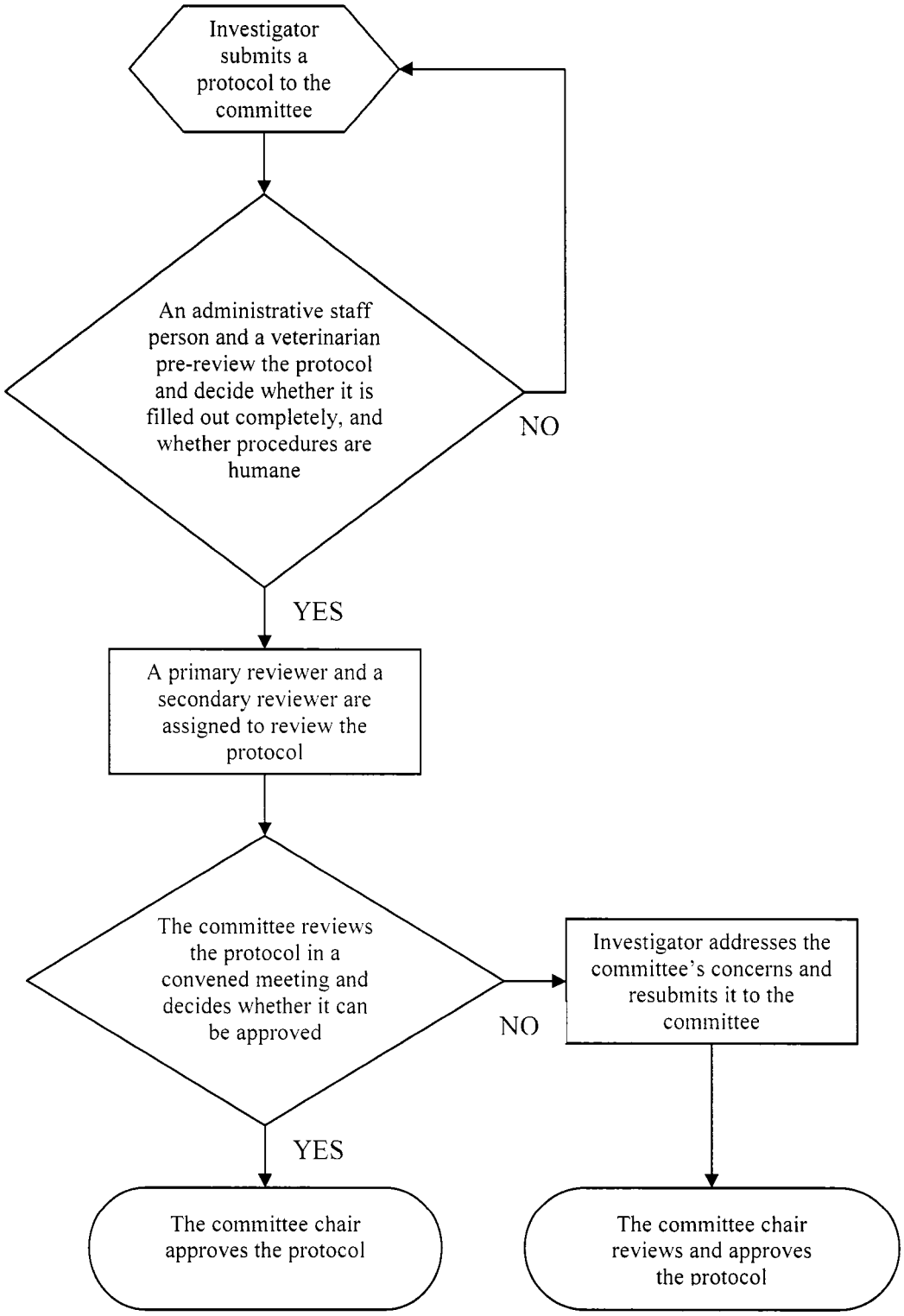

Figure 1. Protocol review process at medical school A.

When the protocol is ready for the committee to review, two committee members are designated as a primary reviewer and a secondary reviewer to review the protocol in depth. Meanwhile, other committee members also have a chance to review the protocol electronically. The committee meets once every two weeks to discuss protocols. During the meetings, primary and secondary reviewers present protocols and their comments to the committee. After discussion, most protocols are sent back to the investigator for further corrections. Protocols are later reviewed again and approved, mostly by the committee chair (Figure 1).

With an average of ten protocols per year, including new protocols and renewal ones, committee B reviews far fewer protocols than committee A. Committee B meets twice a year to review protocols and inspect the school's animal facilities, which fulfills the minimum requirement of the USDA regulations as well as the PHS Policy. The committee chair collects protocols and distributes them to all committee members ahead of the semi-annual meetings. During the meetings, the committee reviews the protocols and decides to issue approvals or not (Figure 2). To expedite the review process, committee members occasionally review protocols individually and e-mail the chair their comments without gathering (Figure 3). Special meetings in which investigators are invited are also held to facilitate communications between the committee and the investigators and speed up the review process.

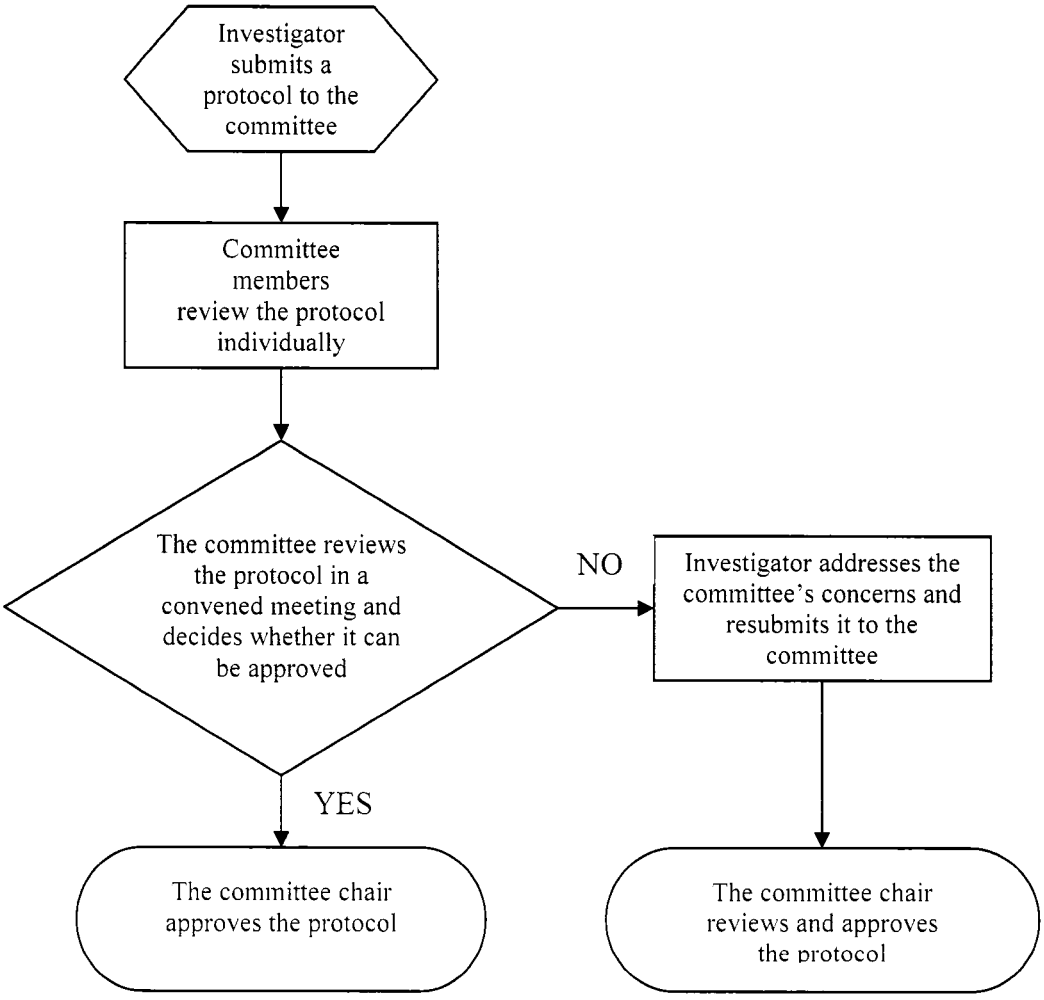

Figure 2. Normal protocol review process at university B.

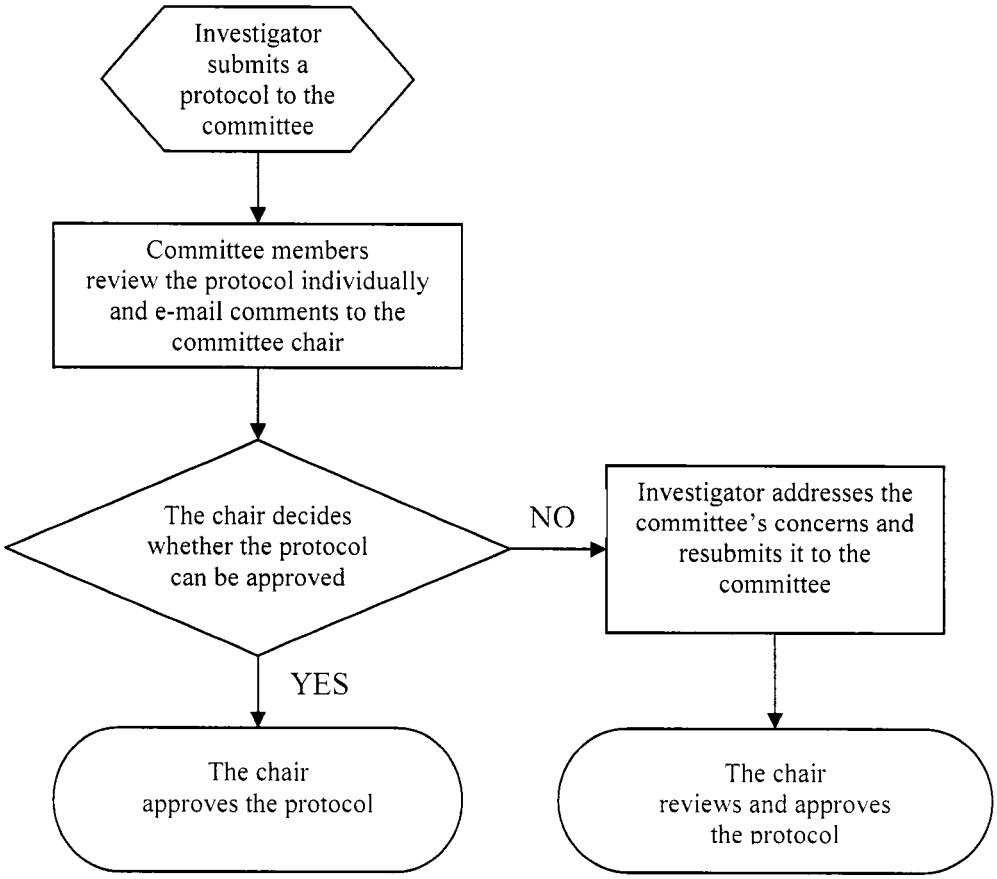

Figure 3. Expedited protocol review process at university B.

The primary difference between the review processes of committees A and B in the United States and committees C and D in Taiwan is that members on committees C and D do not necessarily have the opportunity to look at each protocol. With hundreds of protocols to review annually, committee C in Taiwan also pre-reviews protocols by two committee members, which, at this school, are both veterinarians. One veterinarian checks for protocols' completeness and procedures involving animals; she also makes sure that the school's animal care facility meets the research's requirements. Then, the other veterinarian, the committee's Attending Veterinarian, reviews the protocols' study

design and issues related to the Three R's. These two pre-reviewers decide whether or not protocols should be sent back to investigators for more information. After this pre-screening process, each protocol is assigned to one member to review. This reviewer makes comments for the investigator to address; once this happens, the chair decides whether or not to approve the protocol (Figure 4). Therefore, for each protocol, usually only a maximum of four out of the fifteen committee members get to review it. Protocols are not sent to each member and discussed during regular meetings.

A protocol submitted to committee D is reviewed by one designated member before it is discussed at a meeting. In order to minimize conflicts of interest and personal bias, a member is not assigned protocols which are from the same college he or she belongs to. This committee reviews approximately twenty to thirty protocols per year, most of which are submitted at the end of each year when investigators are applying for grants from the National Science Council. Therefore, meetings are concentrated in November and December. However, for a protocol not submitted in November and December, it is only reviewed by a designated member and the committee chair. Therefore, as with committee C, protocols are not necessarily reviewed and commented on by all committee members.

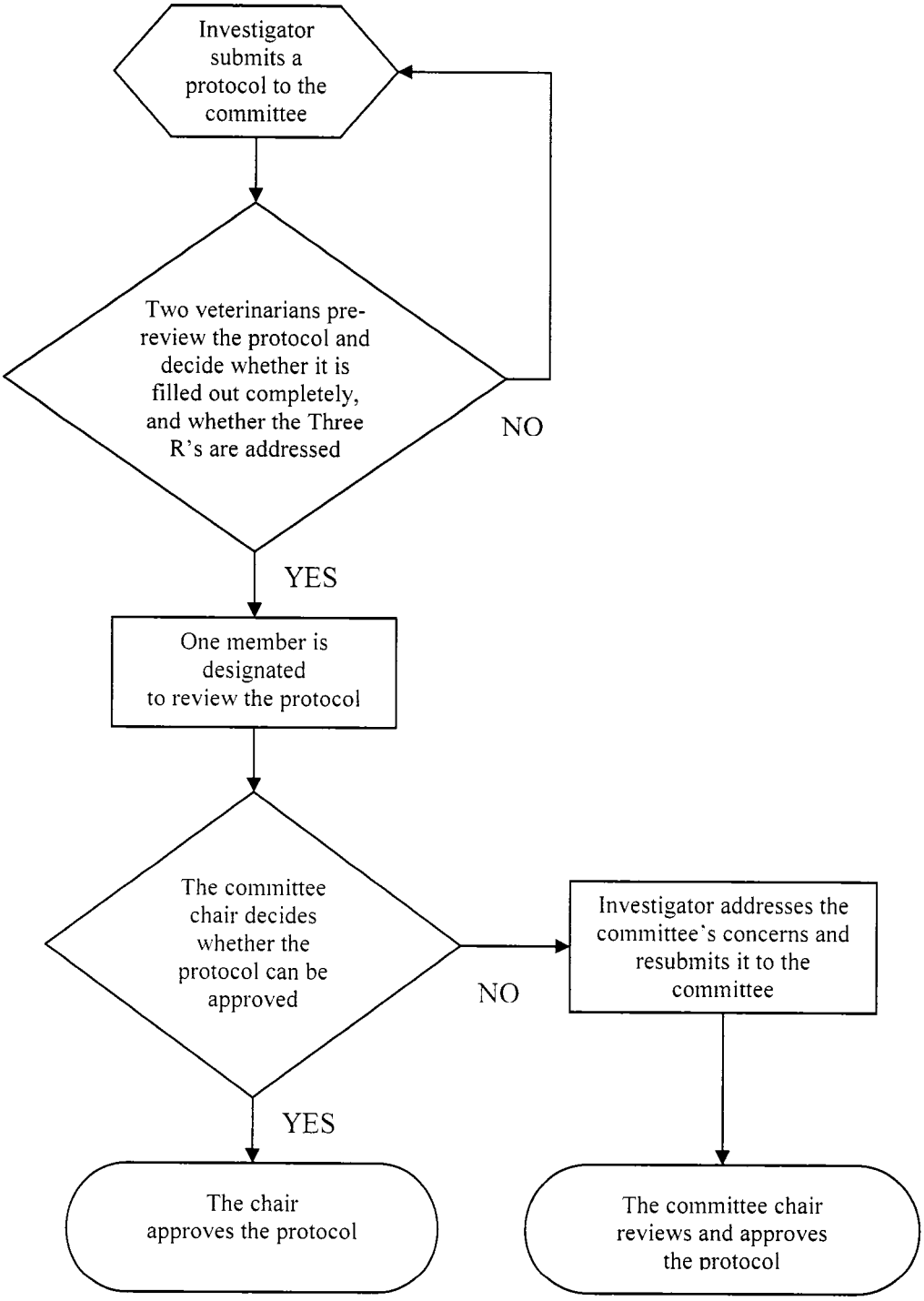

Figure 4. Protocol review process at medical school C.

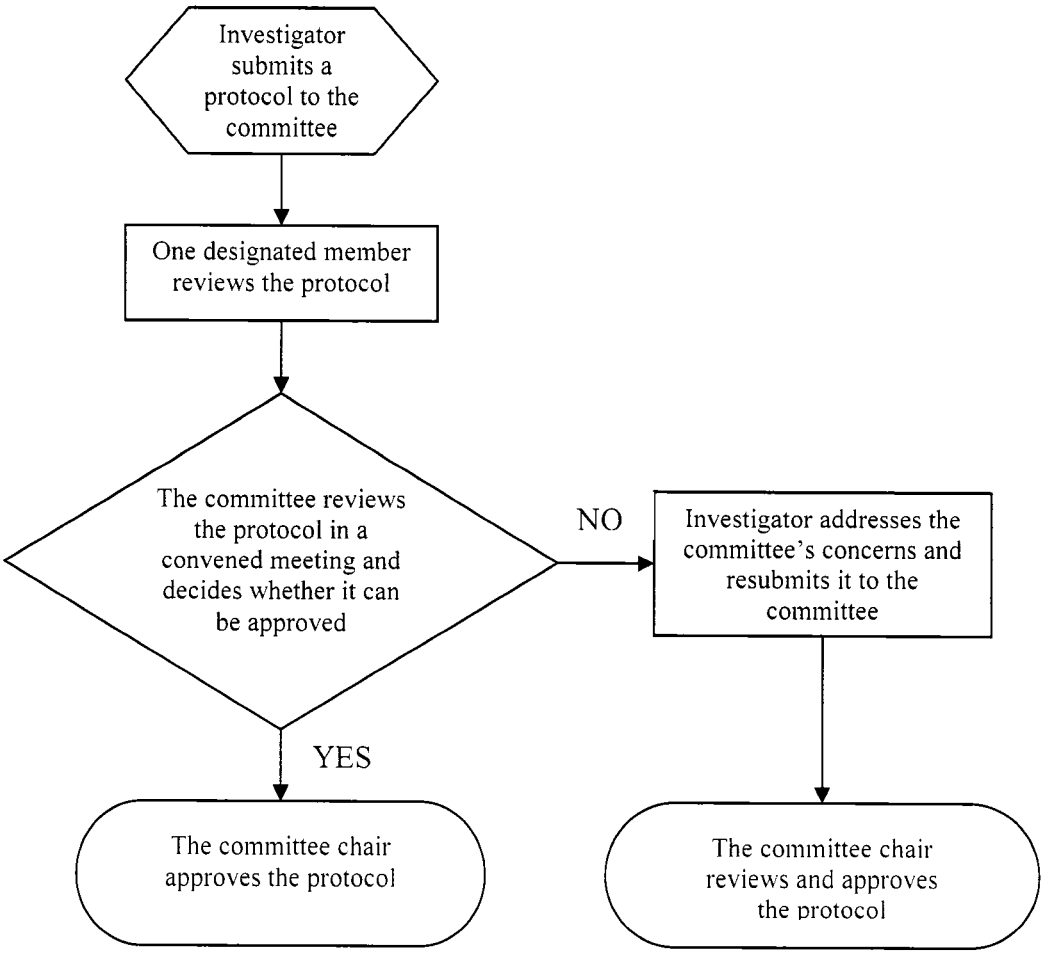

Figure 5. Normal protocol review process at university D.

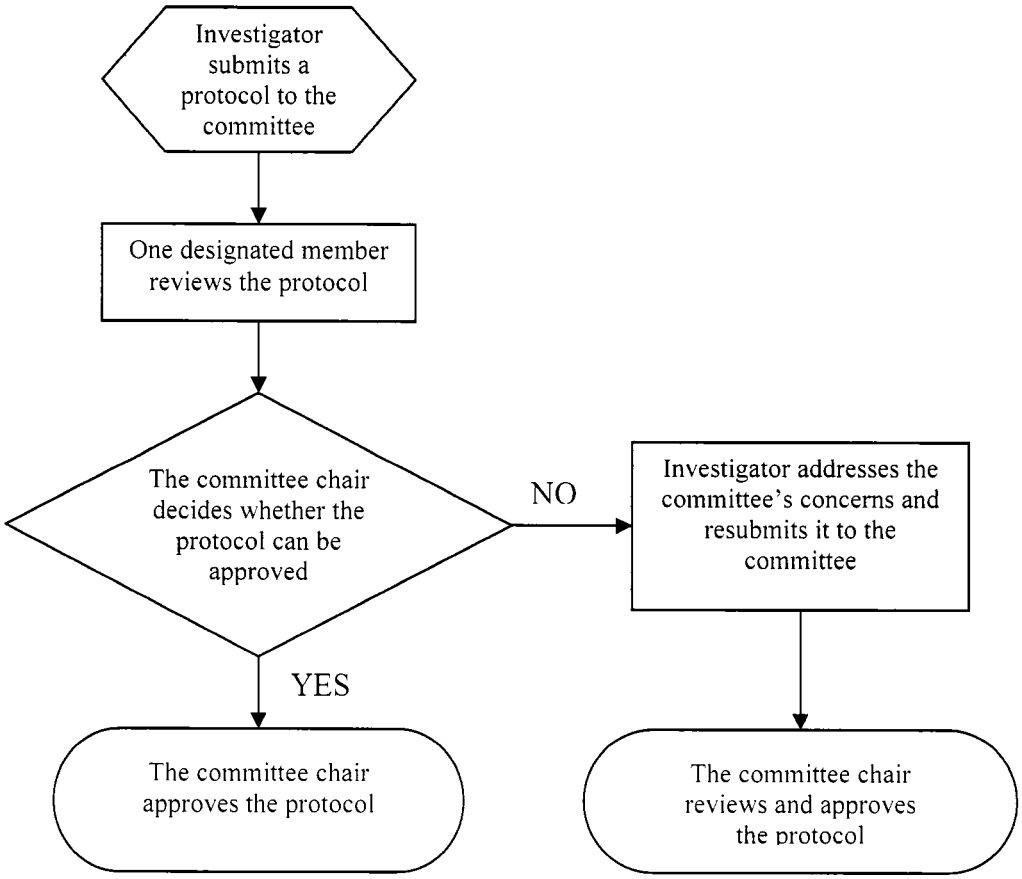

Figure 6. Expedited protocol review process at university D.

Review Priorities

Animal pain. When talking about review priorities, both IACUC and MGAE interviewees were concerned most about animal pain. Managing animal pain is the most important aspect of refinement, one of the Three R's principles. It directly affects the welfare of animals.

In the United States, all interviewees placed great importance on knowing whether or not animals will experience pain and to what extent the pain would be controlled (Table 6). Anesthesia, analgesia, and euthanasia should be incorporated into

research to control animal pain whenever necessary. "Animal welfare is the number one [priority]. So the fact that you are going to use these animals, . . . are you really doing appropriate pre-op analgesics? Are you doing enough anesthesia?"[26] Interviewees in the United States also felt that a monitoring plan for health and signs of discomfort is essential in order to assess and treat the pain appropriately. As a veterinarian at medical school A said:

> The big, big, big, big, big thing I'm concerned about is animal pain. So I'm really watching very carefully if somebody is proposing a study where I think there could be pain or distress. Have they accurately, in my mind, identified all the different things they might do that could cause pain or distress? . . . And then if they've accurately identified it, do I think they plan to manage pain, either to watch for the animals, examine the animals, and also to treat the pain?[27]

The veterinarian further provided details on how animal pain should be treated and identifying criteria for a good plan for monitoring the animals:

> My standard for the pain management is if there's a surgery, I want to make sure that the animals got at least twenty-four hours of post-surgical painkillers that they are being treated with. It depends on what the surgery is and how it's being done. I want to make sure that by the time the general anesthetic is wearing off, he is already being given a painkiller, so as he wakes up from anesthesia, he's already got his opioid or his ibuprofen or similar kind of drug on board. And that people have some commitment for the next three days in particular when there's the greatest potential for pain, that they really have a realistic plan for actually looking at their animals and assessing them.

Weighing animals is an effective and convenient method of assessing the general condition of animals. For example, it is very difficult for an investigator using hundreds of mice to closely observe each animal everyday. However, by weighing them, he can quickly and precisely determine whether they are healthy and comfortable, at least at a

gross level. "If the animal is dropping weight, the observation is, there may be pain," said the veterinarian from medical school A. At medical school A, the loss of weight is not allowed to exceed fifteen percent of an animal's total body weight; otherwise, strong justification for the weight loss must be provided.[28]

Table 6. Aspects of pain control selected by IACUC and MGAE interviewees as their review priorities.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
Pain control and post-procedural care	7	4	**11/11 (100%)**	1	1	**2/14 (14%)**
Anesthesia	2	0	**2/11 (18%)**	5	2	**7/14 (50%)**
Euthanasia	0	1	**1/11 (9%)**	4	4	**8/14 (57%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

In Taiwan, controlling animal pain is also a top priority for MGAE interviewees when reviewing protocols. However, MGAE interviewees adopted a relatively narrower and simpler perspective of pain control measures compared to IACUC interviewees. When talking about pain control measures, no MGAE interviewees discussed using analgesics to reduce pain or monitoring animals for pain and distress. Instead, anesthesia and euthanasia were mentioned by most MGAE interviewees and were considered primary pain control methods (Table 6). A scientist member said,

> What is more important to us is, how we're going to treat him [an animal] so he wouldn't feel much pain during our handling? The best approach is when conducting any surgeries as well as some procedures, we use anesthesia to eliminate his conscious [*sic*]. If he has no conscious [*sic*], he won't feel pain. This is the top principle of our treatment to animals.[29]

Similarly, another interviewee talked about euthanasia, "When the animals need to be sacrificed, you'd better use a fast way to sacrifice them, so there wouldn't be

pain."[30] To MGAE interviewees, as long as a protocol addresses anesthesia and euthanasia, they believed that animal welfare is adequately managed. "If there's no anesthesia in a protocol, we would read it more carefully. Generally, if [the investigator] says he would use anesthesia for every procedure, then there wouldn't be big problems."[31] "As long as he had described [anesthesia and euthanasia in his protocol], then it should be fine."[32]

The Taiwanese government has promoted the use of anesthetics and euthanasia methods since the MGAE system was established. However, the importance of health monitoring, pain and distress assessment, and the use of analgesics have not been addressed. Evidently, MGAE interviewees were unaware of these essential pain control methods.

Animal number. Animal number was selected by the majority of interviewees in both countries to be another essential component of the protocol review process. No specific rule exists relating to the numbers of animals that are required for certain types of experiments; in order to ensure only minimum numbers are involved, IACUCs and MGAEs mainly rely on statistical analyses provided by investigators. For example, one MGAE interviewee stated, "Regarding the animal number, does he have some basis for it? For instance, he says he's going to use 900 animals. But why? Does he describe the reasons clearly? Does he provide background information and sources of the number?"[33] An IACUC interviewee said, "We have them substantiate that and validate that."[34]

Interviewees' scientific knowledge and experience also facilitates the review of animal number. One interviewee in Taiwan said, "Sample size is evaluated according to

our own clinical experience and the investigator's study design."[35] An interviewee in the United States also said, "I use my common sense and my own experience in doing research."[36]

Human health and safety. Interviewees in both countries agreed that animal pain and animal number are the most important issues in protocol reviews. While IACUC interviewees all focused on issues related to animal welfare, human health and safety was also a main concern to a number of MGAE interviewees in addition to animal welfare. To govern the health and safety of all people and animals in the schools, these interviewees pay special attention to the source of animals, the use of infectious or radioactive material, and the handling of animal carcasses.

"The first thing that I review is whether the animals are dangerous, meaning whether you're going to inject some virus into them, and whether this is going to be a threat to the environment."[37] "What I care about is whether the investigator uses infectious material, . . . and the second thing that I pay attention to is whether he uses radioactive material, isotope, which would result in contamination."[38] "We must understand if the experiment would leave any residue in the animal carcasses."[39]

Schools C and D have both had incidents at their animal facilities that threatened human health and environmental safety. At medical school C, an investigator had used radioactive materials on animals without mentioning it in his protocol. As a result, personnel working at the facility and other research animals were exposed to radioactive rays. At university D, mice had been found to have dermatitis, which was not related to any research. "Therefore, we decided that we should incorporate some preventive work

in the future. We [established a protocol which] tracked any diseases in the room. We identified the common diseases and tracked which of them are in the room."[40]

Review of Hypothetical Parabiotic Mice Protocol

Refinement. This protocol involves surgically conjoining two mice to create a parabiotic mouse model (Appendix B). Sixty mice are used to create thirty pairs of the model. The different perspectives on pain control between IACUC and MGAE interviewees were reflected in their review of the post-surgical care for the animals. The post-surgical care in the hypothetical protocol is described as follows:

> Burprenorphine will be administered to each mouse at 0.05mg/kg SQ once the animals begin to show signs of ambulation and every 8-12 hours thereafter as needed for discomfort by laboratory personnel. To facilitate their initial recovery, moistened rodent chow and a heated water blanket will be made available to the mice. Mice tend to fair better as a parabiotic union than other recorded species and little to no complications are expected. Animals will be monitored closely for appetite and lethargy throughout the study.

The majority of MGAE interviewees were satisfied with this post-operational pain management plan (Table 7). "Because he is going to use anesthesia, and he also has post-surgical care methods, it's all out there, so theoretically it should be fine."[41]

The use of the painkiller, burprenorphine, satisfied MGAE interviewees. Several of them said it is good that the investigator uses a painkiller in the research. One veterinarian member explained, "Many professors don't use painkillers because it requires permits, just like anesthetics. Generally speaking, more than eighty percent of effective analgesics for animals are regulated drugs like morphine; therefore many professors feel it's too much trouble to apply for the permits."[42]

This interviewee also commented on the bleeding control during the surgery (as noted in Appendix B). "There's surgical personnel controlling bleeding. Many people don't pay much attention to things like bleeding, but he does." These comments may indicate a serious deficiency in reducing unnecessary animal suffering during experiments at medical schools C and university D.

On the other hand, the majority of IACUC interviewees did not think the pain control and post-surgical care was sufficient. They requested a specific schedule and monitoring criteria for assessing animals' pain, discomfort, and overall well-being (Table 7). "I'm not at all clear on what they are going to do in terms of assessing their animals' well-being for the 48 days after surgery," said one scientist member. "We would like to know that they are going to visit the animals, weigh them, assess them, at regular intervals after the surgery to make sure they're thriving as well as they can."[43]

IACUC interviewees also questioned the use of burprenorphine. It was necessary for them to know the criteria for giving this painkiller to the animals. One interviewee said, "I would want to know what this laboratory personnel would be looking for to determine which discomfort [it] is and at what point they will make the injections. And how often are they observed for that discomfort.[44]

Table 7. Interviewees' attitudes toward pain control in the hypothetical parabiotic mice protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
This protocol does not provide a specific post-op monitoring plan.	6	3	**9/11 (81%)**	1	0	**1/14 (7%)**
This protocol does not provide criteria for humane endpoint.	2	2	**4/11 (36%)**	1	0	**1/14 (7%)**
This protocol has provided adequate pain control to animals.	1	1	**2/11 (18%)**	6	2	**8/14 (57%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

The routine monitoring of animals is important not only because it helps researchers manage their pain and distress but also because when animals seem to deteriorate and start to die, their suffering can be minimized immediately by euthanasia. Several IACUC members requested criteria for early endpoints to be addressed in the protocol. An interviewee said, "At some point you may have to . . . terminate the experiment out of issues related to welfare, but what are the criteria for euthanasia? That's not described here."[45]

Both IACUC and MGAE interviewees were consistent in their review standards for pain management. Monitoring animal health and minimizing pain was the top priority for interviewees in the United States; when reviewing this protocol, they were unanimous in their concern about whether or not the animals would be monitored adequately in order to avoid unnecessary suffering. MGAE interviewees in Taiwan did not advocate monitoring animals or using analgesics; rather, they focused on the use of anesthesia and euthanasia. In their evaluation of this protocol, they were satisfied with the treatment of pain because anesthesia and euthanasia were addressed.

While review of pain management thoroughly reflected interviewees' review standards, interviewees in Taiwan were less critical than those of the United States. This indicates that research protocols in Taiwan can be approved even though routine care procedures and treatment of pain are not addressed for the highest animal welfare standards.

Besides surgical pain, this experiment also causes distress to the mice because by being sewed together, they have no way to escape from their partner and thus must

coordinate movements with each other. Prior to my interviews, committee A had just reviewed a protocol also involving a parabiotic mouse model; therefore, most of its members already knew that the animals can actually adapt to each other well. However, parabiosis was an innovative model to the other three committees. Of these committees, committee C in Taiwan had the most number of interviewees that questioned the psychological impact the experiment causes to the animals. One member said:

> I think their psychological condition will be pretty stressful because each of them used to have four legs, and they can control themselves, but now they have eight legs. . . . It is possible that they are not able to stand up or drink water. Maybe one wants to sleep but the other wants to eat. . . . Another issue is that they may feel very irritated and fight against each other. . . . That's very inhumane.[46]

Interviewees on committee B and D, however, did not pay as much attention to the distress as they paid to the physical pain. They cared mostly about whether each procedure would be conducted following guidelines and regulations; they feel comfortable about the research knowing those guidelines and regulations would be fulfilled. An interviewee on committee D in Taiwan said, "[The animals] would feel more [pain] during the surgery. But in fact the investigator says he would do anesthesia."[47] An interviewee on committee B in the United States further said:

> He has . . . described the mechanism he will use for anesthesia and post-anesthetic recovery for animal analgesia, so I think the amount of pain and distress is fairly minimal. I think that he's done a good job of describing how he's gonna [*sic*] go about surgery, what kind of cautions he might take, and which drugs he's gonna [*sic*] use, both for induction of anesthesia and for post-surgery analgesia.[48]

The reason why interviewees on committee B and D were more likely unaware of the mental distress is probably because of their unfamiliarity with this type of protocol.

Compared to experiments conducted at medical schools A and C, experiments carried out at universities B and D are less complicated and less traumatic to animals. These interviewees might have ignored the animals' mental as well as behavioral discomfort because they were inexperienced in evaluating animal distress associated with such procedures.

Table 8. Interviewees' attitudes toward the distress of animals in the hypothetical parabiotic mice protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
The experiment will affect the mice's mobility and cause great amount of distress to them.	2	1	**3/11 (27%)**	6	1	**7/14 (50%)**
Mice usually adapt to each other quickly and survive well.	5	0	**5/11 (45%)**	0	0	**0/14 (0%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

Replacement. Because this protocol is designed to be problematic in the rationale of using parabiotic animals, interviewees in both countries questioned the justification of conducting such an experiment even though replacement was not one of their preview priorities. The experiment's rationale is described as follows:

> The purpose of this study is to assess the dynamics of passive immunity in the parabiotic mouse model. Little is known about the effects of passive immunity shared between parabiotic pairs for studies of congenital disorders (such as diabetes and leukodystrophies) affected by immune and metabolic function (Partridge, T.A. et al 2002). Specifically, little is known about the migration and infiltration of immuno-globulins between parabiotic mouse pairs. Due to limitations of current systems, it is difficult to ascertain the migration patterns of immunoglobulins *in vivo*. Our approach will be to join an inbred strain (mouse A) with a mouse of a similar background whose phenotype has a protein marker embedded on the globulin chain, SW/Lf2 (mouse B). Through serological testing and tissue harvesting we will be able to quantify the degree of passive immunity between the parabiotic pairs at specific time points in blood and tissues.

> Much is known about the immunological status of Swiss Webster mice (Conboy, I.M., Conboy, M.J., Smythe, G.M. & Rando, T.A. 1994).

Most IACUC and MGAE interviewees felt that this description of rationale did not provide enough information to justify the experiment. "You are supposed to not only tell us how you know that the study is not unnecessarily duplicating existing work but also how you know there aren't alternatives, including what we refer to as refinement alternatives, so less invasive ways of doing this," an IACUC interviewee said. "Why can't you just take some cells from mouse B and inject them into mouse A without sewing the two mice together?"[49] An interviewee from Taiwan also asked, "Do you really have to do it this way? Is there any alternative? . . . I would ask him if this experiment is necessary, if the model has been used before, and what was the reason to use it. If he creates this model, I would ask him why he creates it."[50]

Interviewees further questioned the significance of the research and its relevance to human health. One MGAE interviewee said, "Is this issue important and worth studying? . . . Why is the surgery necessary? Is there anyone reporting that the model can represent a type of human twins for clinical studies?"[51] Similarly, an IACUC interviewee said:

> They want to find out how passive immunity works in parabiotic mice, but they don't say why they want to know how passive immunity works in parabiotic mice. There aren't that many parabiotic mice in the world. So do they want to know that because it relates to how the human fetus gets immunity from the mother? What's the real reason for doing this study? That's missing. The whole relevance to human health and knowledge isn't here.[52]

Both IACUC and MGAE interviewees asked for references to support the use of the parabiotic model. However, IACUC interviewees were more critical about the lack of literature search than MGAE interviewees because regulations in the United States explicitly require a literature search for alternatives to be made. An IACUC interviewee on committee A said:

> I would say that one of the things that we would require here is we would require literature review for alternatives to the use of animals, for the Three R's. And we specify that they have to search at least two databases, and to search for terms that would be relevant to finding something that would either reduce the use of animals, or refine the use of animals, or eliminate the use of animals. . . . We would normally ask them for the databases they searched, the search terms and the date of the search, and . . . something short about the results.[53]

Instead of specifically requesting the literature search for alternatives, MGAE interviewees asked for references proving that the model is an existing, well-established model. "I would ask him to give me some references to read. Actually he has provided some, but if there are more references that can tell us this is a well-established technique in other countries, I probably would be able to accept the entire procedures."[54]

Reduction. This experiment requires a total of sixty female mice. The justification of animal number is described as follows:

> For statistically significant results, we have determined that a minimum of 25 parabiotic pairs of mice should be evaluated for distribution of immunoglobulins. Successful parabiotic union is essential for this study and we will request an additional 10 animals as replacement subjects to insure we have all necessary pairs for this work. Hence, the total number of animals requested for this study is 60 mice.

Besides stating that the number is required for statistically significant results, this description lacks statistical evidence to support the statement. Most interviewees considered animal number to be one of the most important aspects to review in a protocol; however, with the exceptions of members on committee A in the United States, the majority of interviewees on committees B, C, and D accepted using sixty mice without asking for statistical justification (Table 9). "He has explained very clearly on how many animals he wants, so the number should be reasonable."[55]

Table 9. Interviewees' attitudes toward the number of animals requested in the hypothetical parabiotic mice protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
The animal number is not justified.	4	0	**4/11 (36%)**	3	0	**3/14 (21%)**
The animal number is okay.	1	3	**4/11 (36%)**	6	4	**10/14 (71%)**
I don't look at animal number.	1	0	**1/11 (9%)**	0	1	**1/14 (7%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

Relying on scientific knowledge and research experience instead of sound statistics and references in assessing animal number can be problematic. "I'm sure the number of animals is not too big. He's not going to use a large number of animals."[56] Compared to what interviewees normally review, the number used in this hypothetical protocol is relatively small. "The number is reasonable. Sixty. Some of our research uses one or two hundred animals."[57] Some interviewees even considered the number to be too small. "I suspect that there will be no useful data from just a few animals."[58]

On the other hand, some interviewees believed that too many animals are required for the experiment. "My first take is that the number is large, and I would require them to

re-justify the number."[59] "I think sixty mice would be a bit too many. . . . He can provide more information about the numbers of animals that other people use [in this type of research]."[60]

One interviewee in each country did not consider reviewing animal number to be their responsibility. The interviewee in the United States said, "I didn't even look at the number of animals used. I was looking at the protocol; I am looking at the pain and distress for the animals [and] the magnitude of the surgery."[61] The interviewee in Taiwan said, "My understanding is that, on our committee, animal number is not a factor to assess. We think that should be reviewed by the National Science Council."[62]

As one of the Three R's principles, reducing the numbers of animals to a minimum affects animal welfare and is a crucial aspect that IACUCs and MGAEs should review in protocols. In the United States, if one IACUC member does not review animal number, other members on the committee may cover that since protocols are always reviewed by more than one member and are often discussed during a meeting. However, this can be a major problem in Taiwan because many MGAEs, including committee C and sometimes committee D, assign only one or two members to review a protocol without assembling to discuss it. Therefore, if members on a committee vary in their review criteria and standards such as animal number, the committee can be inconsistent in their review of each protocol.

The review of animal number in this experiment demonstrates that although most interviewees in both countries claimed that they care about whether minimum numbers of animals would be used, they did not necessarily ask for evidence justifying the number.

Instead, they often relied on their own scientific knowledge and research experience to assess the number. This can lead to different review results among members as well as committees since no sound statistical analysis is used during their reviews. In this case, excessive numbers of animals may be used in research.

Review decisions. Most interviewees in both the United States and Taiwan decided that the protocol should be sent back to the investigator to address deficiencies related to the Three R's before getting approval (Table 10). Some interviewees on committee A recommended a pilot study be conducted, which is a good way to evaluate the animals' condition prior to the experiment being launched. One of them said:

> I'd almost recommend that first couple of animals that are done by this group be watched by the compliance people. And we do this quiet often. And see how the animals do and subsequently in their recovery, whether this is adequate enough or whether there are other things [that] could be done. So the first animals would be sort of like pilot animals, and then they would be followed up by our compliance people who have experience in post-op recovery of rodents. They could tell us. They would give us feedback that this is good enough or not good enough.[63]

Table 10. Interviewees' decisions about the hypothetical parabiotic mice protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
This protocol needs to be sent back to the investigator for more information.	4	4	**8/11 (73%)**	5	2	**7/14 (50%)**
A pilot study should be conducted first.	3	0	**3/11 (27%)**	0	0	**0/14 (0%)**
This protocol can be approved now.	0	0	**0/11 (0%)**	1	2	**3/14 (21%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

While IACUC interviewees all agreed that the protocol needed to provide more information to address the Three R's before getting approved, several MGAE

interviewees approved the protocol (Table 11). Even though one of the latter questioned the necessity of conducting parabiosis research and the animals' level of pain and distress, he nevertheless approved the protocol. According to him, "Basically my concerns are just what I mentioned before. I think other parts are good. The descriptions are very detailed and are clearer than what we usually see. . . . My feeling is that this can be approved."[64]

Those interviewees that approved the protocol were all satisfied with descriptions in the protocol. In fact, most MGAE interviewees felt that the protocol was well-written and more detailed than protocols from their schools (Table 11). However, according to IACUC interviewees, it was less detailed, especially in post-surgical monitoring and justification of conducting the experiment.

> We expect more indication about the rationale for using the animals. . . . They do cite several papers, but at no point do they indicate whether these measures can be done in vitro, as opposed to in vivo. . . . We have a particular section on minimizing risk of physical and psychological harm to the animals. And although that's included with regard to analgesics and sedatives, that type of section would have included information on how closely the animals are monitored for pain and discomfort and what the criteria is for pulling them away from the study. So . . . the kind of things I have questions on would be the things we've asked the researchers to include normally in our IACUC.[65]

Table 11. Interviewees' perceptions of the amount of information provided in the hypothetical parabiotic mice protocol.

	United States			Taiwan		
	A	B	Total	C	D	Total
This protocol is less detailed than protocols from my school.	7	2	**9/11 (81%)**	0	0	**0/14 (0%)**
This protocol is more detailed than protocols from my school.	0	0	**0/11 (0%)**	3	4	**7/14 (50%)**
This protocol contains same degree of descriptions as protocols from my school.	0	0	**0/11 (0%)**	5	0	**5/14 (36%)**
This protocol is well-written and detailed.	1	1	**2/11 (18%)**	6	4	**10/14 (71%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

The results indicate that protocols at schools C and D in Taiwan are less detailed than those at schools A and B in the United States. MGAE interviewees are likely to approve protocols that would not be accepted by IACUC interviewees. Moreover, it is possible that a protocol is approved even though its MGAE reviewer still has concerns about it. Their review standards are not as high as those of IACUC interviewees. It is more likely that a protocol is approved by an MGAE when it is still problematic in addressing the Three R's than being approved by an IACUC.

Review of Hypothetical Wild Bird Protocol

Refinement. This protocol involves capturing one hundred common, non-native birds from the wild and confining them individually for ninety days (Appendix C). In order to understand their food selection behavior, the birds would be provided with three separate servings of live crickets, pesticide-killed crickets, and frozen crickets all together every four days. For the other three non-experimental days, they would be fed with normal wild bird food.

As with the parabiotic mice protocol, the health monitoring and pain control of birds was of great concern for many interviewees in the United States (Table 12). Their major concerns included what adverse effects the experiment would cause the birds, and if the birds do become ill, what the criteria and methods would be for early endpoint. "If they ingested this insecticide, it may make them ill before the three months are up. So there is no monitoring in [*sic*] these animals. So that would be a concern to me. No monitoring and no documentation of their well-being on a regular basis." She further added, "What kind of adverse effect they might expect, and what will they do if they encounter these adverse effects, and what are the criteria for euthanasia?"[66]

In Taiwan, similar to the review of the parabiotic mice protocol, few interviewees recommended monitoring for the birds.

Table 12. Interviewees' attitudes toward pain control in the hypothetical wild bird protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
The birds need to be monitored for signs of discomfort.	4	3	**7/11 (64%)**	2	1	**3/14 (21%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

Experimental design. There had been no protocol involving wild animals submitted to committee C and D in Taiwan before my interviews. In the review of this protocol, MGAEs showed great interest in the experimental design and procedures due to their unfamiliarity with the type of protocol and the species used in it. Compared to IACUC interviewees, MGAE interviewees paid more attention to the experimental design than on the pain and distress management of the animals (Table 13). "How would the crickets be caught, and what is the amount of pesticide sprayed on them? How much time would the

crickets need to die? Would the experiment start right after they die, or would it wait for a while? I think he needs to explain these."[67]

MGAE interviewees also questioned the rationale and scientific value of this experiment. They were concerned about whether the experimental design reflected the pollution of the pesticide and bird behavior in the wild. "Does the experiment truly represent conditions in the wild? Maybe there are times when the birds only have dead crickets to eat. This experiment would not reflect the actual conditions the birds might encounter in the wild."[68] "Does the experiment simulate the level of contamination in the wild? . . . You should catch a few bugs from the wild and find out how much pesticide is in the bugs."[69]

MGAE interviewees were more diligent in seeking refinement alternatives than IACUC interviewees. Even though their questions focused mainly on experimental design and procedures, they employed their scientific knowledge to search approaches to minimize harm to the birds. "If you want to know the bug selection habit of a specific bird species, . . . you probably need to observe them directly in the wild."[70] Another interviewee added, "We can catch some birds from the wild and do an analysis on the levels of chemicals in their bodies. . . . We can also find dead birds and test the level of pesticide in their blood."[71]

Table 13. Interviewees' questions about the experimental design in the hypothetical wild bird protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
What is the amount of pesticide in each cricket?	2	0	**2/11 (18%)**	5	0	**5/14 (36%)**
Does the experiment reflect the concentration of pesticide in natural environment?	0	0	**0/11 (0%)**	2	1	**3/14 (21%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

Replacement. The species of bird for this experiment was chosen because of its non-native status, abundance throughout each country, and omnivorous foraging behavior. This rationale was not considered an adequate justification by the majority of interviewees in both countries. Concerned about the relevance of the species to the experiment, an MGAE interviewee asked, "Does the bird have a high mortality rate [in the wild] due to the intake of the pesticide? If it does, then of course this study is worth doing. But if it doesn't, then it's very strange that you want to catch and kill a hundred of the species."[72] One IACUC interviewee further commented,

> Just because they're wild non-native animals doesn't necessarily justify the experiment because it's like saying "I'm gonna [*sic*] use rats because they're usually abundant and they're pests and people don't like them." . . . It's sort of implying here the same thing to starlings that "I'm gonna [*sic*] use starlings rather than a native bird because simply there's lot of them down there that are pests and they are not welcome here," and that's not a justifiable reason for using that particular species. It should be more relevant to the species itself with a reason, like you know, like I say "Okay, I'm gonna [*sic*] capture some bald eagles and do this experiment because they're endangered and threatened.[73]

Another issue related to the selection of the species was that the protocol did not address whether information gathered from the species reflected the common behavior of other species. "I don't know enough about bird species to know whether or not wild

starlings can be generalized to other birds [if] you really want to know about endangered species."[74]

Table 14. Interviewees' attitudes toward the animal model used in the hypothetical wild bird protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
The animal model is justified.	3	1	**4/11 (36%)**	3	0	**3/14 (21%)**
The animal model is not justified.	4	3	**7/11 (64%)**	4	1	**5/14 (36%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

Conversely, several interviewees in both countries accepted using the species because of its abundance and non-native status. "It [the model] is good in terms of they're a common species and abundant."[75] "He says that the animal is a common species, so I would probably accept his use of it."[76] This indicates that each member's review standards for animal model may vary; intra-committee inconsistency may occur when members review justifications of an animal model.

Some MGAE interviewees also expressed concern over using wild species instead of commercially bred laboratory animals. Their attitude reflects the Chinese perspective that distinguishes wild animals from animals bred by humans. One interviewee said:

> Do you have to use wild birds? Is it possible to use domestic ones? Domestic animals and wild animals are different in their meanings to the animal kingdom and nature. . . . For instance, killing a cow for food is different from killing a wild buffalo for food. What I'm trying to say is that regarding animals that you raise, the purpose that you raise them is for experiments. So would it be better if you use domestic birds instead of wild birds in this experiment? . . . It would be more humane to use domestic birds.[77]

Although few interviewees considered using wild birds to be inappropriate, this perspective is unique to Taiwanese interviewees. In the United States, interviewees did not consider wild animals to be different from laboratory animals and, therefore, their attitudes were not against using wild birds.

Reduction. This experiment requires the capture of one hundred birds from the wild. Without providing information regarding study design and statistical analysis, the protocol merely states that a hundred animals will be used in order to obtain statistically significant results (Appendix C).

Almost all interviewees in both countries strongly questioned the number of birds that would be used, regardless of the species' abundance and non-native status. An IACUC interviewee said, "They didn't explain why they need a hundred birds. That's a lot of birds . . . for a fairly simple study."[78] Most MGAE interviewees further emphasized that detailed information about the experimental design is needed to justify the number. "He didn't explain how he's going to use the one hundred animals. . . . There is no information about the grouping of the animals. . . . I can't even know if one hundred is okay because he didn't address the study design."[79]

Review decisions. Most IACUC and MGAE interviewees decided that this protocol should be sent back to the investigator to address the health monitoring and criteria for humane endpoint, the experimental design, the rationale of conducting this experiment on this bird species, and the number of birds requested (Table 15).

Table 15. Interviewees' decisions about the hypothetical wild bird protocol.

	United States			Taiwan		
	A	**B**	**Total**	**C**	**D**	**Total**
This protocol needs to be sent back to the investigator for more information.	5	4	**9/11 (81%)**	8	2	**10/14 (71%)**
This protocol can be approved now.	1	0	**1/11 (9%)**	0	1	**1/14 (7%)**

Total = Total number of interviewees in each category/total number of interviewees in each country.

Interviewees in the United States also required a literature search to address the Three R's principles, such as to prove that the experiment did not duplicate other previous research. An IACUC interviewee said, "We require more information than this on all of our protocols. . . . The very first thing it's missing here is the literature research for alternatives, the Three R's search."[80] However, no MGAE interviewees asked for such literature search even though they were skeptical about the study design and wanted to seek more alternatives.

Regulations and the Protocol Reviews

Lack of review criteria. The Taiwanese government, along with the Chinese Society of Laboratory Animal Sciences, has spent a great deal of effort educating MGAE members in the proper use of anesthetics and humane euthanasia procedures on each species of laboratory animals. MGAEs are also required to submit annual reports to COA on euthanasia methods used. These efforts are quite successful because anesthesia and euthanasia were the top concerns of most MGAE members interviewed in this research. Guidelines established by the government along with the Society have also become the

primary reference for conducting anesthesia and euthanasia in Taiwan. However, the government has not addressed the importance of health monitoring, pain and distress assessment, and the use of analgesics. Therefore, MGAE interviewees' review of pain control mainly focused on anesthesia and euthanasia; almost all of them were unaware of alleviating pain through a proper monitoring plan and the use of analgesics.

Conversely, in the United States, the importance of pain and distress monitoring was well-recognized by interviewees; all of them required pain and distress monitoring to be addressed in the hypothetical protocols. The PHS provides thorough guidelines for pain and distress assessment and management. The *Institutional Animal Care and Use Guidebook* emphasizes the necessity of observing animals and recognizing signs of pain and distress (OLAW 2002). Moreover, the USDA requires pain classification in annual reports. IACUCs and investigators must accurately identify the amount of pain animals experience, following a scale of B, C, D, and E, in which category B is for animals that are not yet used in research, C is for animals having no pain or distress, D is for animals having relieved pain or distress, and E means animal pain and distress are not relieved due to research purposes. This pain classification is effective in helping IACUCs understand what is going to happen to animals. "That tells me what types of procedures would be done to the animals, and how much it will affect the animals."[81] It also facilitates IACUCs in assessing whether pain and distress are reduced to a minimum. One interviewee said, "We obviously scrutinize category E much more than we do in the other categories, and make sure that we are satisfied why they cannot use like post-op analgesics or whatever to relieve pain and discomfort."[82]

Currently the standard protocol form created by the COA and used in most research institutions in Taiwan does not require this pain and distress monitoring. One interviewee said, "People don't have the habit [of addressing criteria for humane endpoint], and formats of protocol do not include that part, either. . . . It must be defined clearly what conditions an early euthanasia should be conducted on animals. . . . It is very important to let people know that when certain conditions happen, you must euthanize animals for their welfare."[83] Her comments demonstrate the urgent need in Taiwan to modify the standard protocol form to address criteria for administering analgesics as well as conducting early euthanasia.

The reviews of the wild bird protocol indicate that MGAE interviewees tended to evaluate protocols from a scientific standpoint, while IACUC interviewees reviewed protocols mainly from an animal welfare perspective. The protocol includes minimum information about the rationale of conducting the experiment, and MGAE interviewees were more critical about the experimental design and the study's significance than IACUC interviewees. Being concerned about the science, they also sought more alternatives than IACUC interviewees did. On the other hand, IACUC interviewees mainly focused on issues affecting the pain and distress of animals, such as the lack of health monitoring and humane endpoint.

MGAE interviewees reviewed this protocol from the standpoint of science partly because they were unfamiliar with research that involves the use of wild animals. According to interviewees, whether the care and use of wild animals in research are governed by MGAEs is unclear in Taiwan. Committees C and D had never received

protocols involving wild animals prior to my interviews, therefore the species chosen in the wild bird protocol and the experimental design were unusual to the interviewees. Having no experience in evaluating animal welfare in such protocols, they used their scientific knowledge to assess its scientific design and value.

Moreover, detailed and specific review criteria for the Three R's have not been established in Taiwan. The Animal Protection Act merely states that animal number should be reduced to a possible minimum, and procedures should cause the least amount of pain to animals. Since the language of the APA is rather limited and no further guidelines and criteria have been developed, MGAEs can only rely on personal knowledge and standards to review protocols.

Relying on merely personal scientific knowledge is inadequate because if a committee receives a protocol that does not fall under any committee members' expertise, the committee may have difficulty reviewing its use of animals. One interviewee said, "Now the size of our committee is limited to fifteen members. I think this potentially could be a shortcoming because no matter how competent and how expert we are, there are still some areas that we are not familiar with."[84] Another interviewee on committee D has already found that the lack of review guidelines and criteria make it difficult to assess whether the Three R's are addressed. One interviewee said:

> To assess whether an experiment really needs to use animals requires very specialized expertise. Only people whose expertise is in the same field would know whether the experiment can be done in other ways that don't require the use of animals. . . . We can only ask members who have conducted similar experiments before whether there are other alternatives. . . . But it's usually very difficult to determine that an experiment should not be conducted. . . . We really have this kind of difficulties. We almost never use this

> reason to reject a protocol. . . . The reasons why we ask investigators to revise protocols are usually because the animals would endanger [human health and environmental safety] or the euthanasia methods need to be changed.[85]

Intra-committee inconsistency. Intra-committee inconsistency occurred in the reviews of animal model and animal number which are involved in the hypothetical protocols. While the majority of IACUC and MGAE interviewees were critical of the protocols' justifications of conducting the experiments on the animal models presented, some interviewees in both countries accepted the rationale of using the models. Even though review criteria exist in the United States, each IACUC member may still have different review standards.

The reviews of animal numbers in the hypothetical protocols demonstrate that both IACUC and MGAE interviewees tended to use scientific knowledge and research experience in evaluating animal number. Interviewees on committee A performed the best review of animal number among the four committees by requiring sound statistical justifications for animal numbers required in the protocols. Interviewees on committees B, C, and D also unanimously questioned the animal number in the wild bird protocol since the number was fairly large and the experimental design was lacking; however, most of them accepted the number required in the parabiotic mice protocol without asking for statistical justifications. Instead, they assessed the number using their own knowledge and experience in research, and this resulted in inconsistent judgments among each member.

Although one member on committee C in Taiwan is a statistician who helps review animal number in protocols, she does not review all protocols. Only protocols

with large numbers of animals or complicated statistical analysis will go through her evaluation. Since other members on the committee tended to use their own judgments to assess animal number, animal number is not necessarily governed and reduced to a minimum, and intra-committee inconsistency regarding animal number is still a likely occurrence.

To minimize intra-committee inconsistency in protocol reviews and achieve the best animal welfare practices, protocols should be reviewed by each committee member. In the United States, regulations give committee members the opportunity to review and comment on every protocol even when the designated member review is employed. However, this requirement has not been established in Taiwan. Protocols submitted to committees C and D are often reviewed by only designated members, not the full committees. Therefore, intra-committee inconsistency is more likely to occur in Taiwan than in the United States.

Differences between Medical and Non-medical Schools

Due to the different amounts of research at the schools, there are several differences in the protocol review systems between medical schools, A and C, and non-medical schools, B and D. Medical schools A and C both develop hundreds of protocols each year; therefore, they have large committees consisting of more than ten people. They also have on-site veterinarians serving on the committees to supervise and provide recommendations on the care and use of animals. University B and D develop fairly small numbers of protocols each year; comparably, the size of their committees are relatively small. To comply with regulations, committee B has an attending veterinarian.

However, he is not a staff of the animal facility; therefore, animals in the facility are not monitored by veterinarians. Committee D does have a veterinarian in the animal facility; however, he is not a member of the committee because MGAEs are not required to have veterinarian members.

Committee A and C both have a pre-review system in which protocols are checked for completeness and procedures involving animals before they are assigned to other members. Committee D designates one member to conduct a review before convening with the other members to discuss it. Committee B, which has the least number of protocols annually among the four committees, does not conduct pre-reviews before protocols are discussed at meetings.

There is no difference between schools having large numbers of protocols and those having small numbers regarding the review standards of the hypothetical protocols with the exception of the review of mice's distress in the parabiotic mice protocols. Interviewees on committees B and D paid less attention to the animals' distress than interviewees on committees A and C likely because committee B and D have less experience in reviewing experiments that are complicated and traumatic to animals. Thus, they might ignore animal distress associated with such procedures.

EFFECTIVENESS OF THE PROTOCOL REVIEW SYSTEMS

Relevance to Research Question

Although the United States and Taiwan have similar systems for reviewing animal protocols, this chapter explores similarities and differences of interviewees' perceptions of the efficacy of the protocol review systems in each country (Research Question 5). It also analyzes the influence of regulations and cultural values on the systems' effectiveness in governing the welfare of laboratory animals.

Awareness of Animal Welfare

Comparing perceptions of the protocol review systems' effectiveness between the United States and Taiwan, interviewees in Taiwan perceived their system to be effective in educating investigators on the importance of animal welfare, while interviewees in the United States found that their system cannot be effective without a diverse, experienced, and active membership.

In Taiwan, most MGAE interviewees considered the review system to be effective in raising investigators' awareness of animal welfare. One MGAE interviewee said, "I think the most important contribution [of the review system] is that it awakens people's perspective to treating animals nicely."[86]

One interviewee described Taiwan's use of animals prior to the establishment of the system. "At the time when there was no review for protocols, people were very sloppy in using animals. And what's more, we didn't know if those experiments were reasonable. . . . First, there was no control on animal number. . . . Second, investigators did not respect animals because it was so easy for them to get animals."[87]

Now, with MGAE oversight, investigators can no longer conduct research without taking animal welfare into consideration. "Through the MGAE review system, we have certainly made teachers and other animal users cautious in their use of animals because they realize that they can't use animals indiscriminately. The only way to conduct animal experiments is to go through this review process."[88]

The review system is also effective in educating investigators on handling animals properly and humanely. "In our protocols we have a statement where we tell investigators which anesthetic to choose for their animals, and there is a list of anesthetics for them to select. They gradually understand what a good anesthesia method is."[89] Another interviewee talked about his own experience:

> I used to perform a surgical disclosure on mice when I needed to sacrifice them. That means you press the neck and pull it, breaking the spine, so the animals become paralyzed and die. . . . It was fast, but to the animals, they died because they were injured seriously. Now we put them into a box with CO2, and according to our attending veterinarian, they are anesthetized and they die peacefully and unconsciously. This makes no difference to my experiment, but it shows respect to a living being.[90]

Composition of Membership

In the United States, most interviewees perceived that the composition of committee membership and members' active participation make the IACUC protocol review system effective. Scientist members, especially senior scientists, are essential to a committee because their scientific knowledge and experience enable them to assess the rationale and significance of an experiment and the necessity of using animals. They also provide a high level of peer interaction for investigators because they not only oversee procedures involving animals but also help investigators conduct high-quality research.

An IACUC interviewee described a benefit of having senior scientist members on a committee:

> When another senior scientist submits a proposal and starts getting pushy about "You have to approve it this way," they're the ones who will stand up and say, "No, I've done NIH grants, I know how to do science, and this isn't some staff veterinarian that you can bully around. I'm your peer, and I'm telling you that you haven't done a good job of justifying why you want to do it this way.[91]

Several interviewees on committee A perceived nonaffiliated members to be very valuable to the committee. The committee has three nonaffiliated members; two of them have scientific backgrounds and the other one is a nonscientist. Because they are not familiar with animal research, they offer a different perspective from those members who have used thousands of animals in research and reviewed thousands of protocols. Thus, they contribute to the committee by asking fundamental questions that are often ignored by other members. One interviewee said, "They sometimes bring up the most germane and important points in the discussion."[92]

It is extremely important to have veterinarians on a committee because no one understands the needs of animals more than veterinarians do. Hence, their participation in the review process is crucial to overseeing animal health and welfare. A veterinarian on committee A said,

> One of the things I think is effective is that a veterinarian gets to say what his or her opinion is about how the study should be done before it ever starts. That to me is a real change because I started working with lab animals before there were IACUCs, and the attitude then was that vets keep the animals healthy, but once the experiment starts, vets can just go mind their own business. "I'm a scientist; I know what I'm doing. I'll do my experiment the way I think I should do my experiment." Now, vets have much more of a

> voice on things like what's a good anesthetic to use, is this a good way to do this surgery, and what's the good painkiller to use.[93]

Since it is composed of members with different backgrounds and expertise, a committee is able to more effectively review different types of experiments and provide recommendations regarding animal care and use. An IACUC member said, "It's effective because you have multiple individuals with very different backgrounds in their training and in their experience reading the protocol independently and then coming together as a group. And if one person has questions, someone else within the committee may be able to answer those questions or help articulate what is going on within the application."[94]

Besides the composition of membership, interviewees in the United States also agreed that their protocol review systems are effective because members participate in the review process actively and enthusiastically. One member on committee A said, "We have a committee that's very interested. That is, they do a thorough review as opposed to just a person who reads it through once and says okay. We have an interested committee who's dedicated to do [*sic*] a thorough review."[95] An interviewee on committee B attributed the efficacy of the committee to the positive interactions between members. "I think we communicate well with each other, and I think there's a good deal of trust among the committee members that we are usually in agreement but people aren't afraid to disagree on the committee. . . . It's well-running; we just have a good group of people running that committee."[96]

Submissions of Protocols

In the United States, committee members were most frustrated with investigators' careless attitudes when preparing protocols. Most interviewees on committee A felt frustrated that many protocols are confusing and poorly written. Although the committee requires protocols to be written in lay language, some investigators still fill out protocols with research jargon and technical terms that are very difficult to understand. This is often corrected by the input of those nonaffiliated members on the committee. The nonaffiliated, nonscientist member said, "For my comments, often they are asked to clarify, simplify, and define technical terms or don't use technical terms in the objective section."[97]

Some investigators write in such a confusing manner that no one on the committee can figure out what they want to do. One interviewee on committee A commented, "The standard protocol forces you to organize each section, but within the section, if the investigator doesn't care, they can put things in such a confusing way that we don't understand what they are doing."[98] According to several interviewees, this also happens when English is not the investigators' native language.

To interviewees on committee B, the most frustrating aspect of the review process was the lack of information in protocols. For instance, some investigators do not provide an appropriate literature search for alternatives, which should include the date and keywords of the search. Euthanasia is also commonly overlooked by investigators. "The number one [problem] is always the alternatives haven't been clearly stated, and that

there is no indication how they are going to sacrifice the animals," an interviewee on committee B said. "It just seems careless in a certain way."[99]

A number of MGAE interviewees in Taiwan, both on committee C and D, also agreed that the lack of detail in protocols often makes their review difficult. This lack of detail is associated with both the negligence of investigators and the lack of detailed submission requirements. "Many professors think that they just need to slightly describe the research. For example, they may not clearly provide the dosage of anesthetics such as ketamine and pentobarbital."[100] Another interviewee added:

> In fact, sometimes I don't quite understand each experimental procedure in a protocol. Because our requirements for investigators are pretty simple, they write protocols in a simple way. And now we further require them to submit an abstract of the research along with the protocols, but you know, . . . it's still very difficult to understand the entire experiment from merely the one-page abstract. So if I'm not familiar with the research field, I can't really understand the procedures from only the title and abstract of the experiment.[101]

Both IACUC and MGAE interviewees suggested that adequate training and guidance in animal care and use for investigators is necessary to solve the lack of information and clarity in protocols. Investigators need to be educated about writing protocols and conducting research that comply with existing regulations. An interviewee in the United States said, "[The lack of information] does [happen] for each new person coming in. And once you train them, it's perfect."[102] Another interviewee in Taiwan added, "It's very important to have educational programs. After being educated constantly, you'll be brainwashed and think 'Yeah, I should do so.'"[103]

Ongoing Projects

The lack of oversight for ongoing projects is the most serious deficiency of the MGAE protocol review system perceived by Taiwanese interviewees. Most of them said that because their committees do not have a mechanism to oversee ongoing projects, it is very difficult to know whether these projects are conducted in compliance with their approved protocols. An interviewee on committee C said, "Things in protocols can be changed; you can always have investigators revising the protocols. But we don't know whether they really follow the protocols or not. . . . They can always write perfect protocols following everything you require to get approvals, but how they are actually going to do the experiments is another story."[104] Another member on committee D further added:

> Because the review system is an honor system, if investigators really don't want to follow the protocols, we can do nothing about it. We are not a law-enforcing agency, we don't have a police, and we don't have something like an environmental protection team to supervise the conduct of those research. So we just provide opinions from the standpoint of reviewing protocols and decide whether to approve protocols or not; after we issue the approval, we don't have the ability of enforcement. This is a problem of the design of the system.[105]

Currently in Taiwan, the primary approach for detecting investigators' noncompliance is through the daily care and observation of animals by the staff in animal facilities. As mentioned in the previous chapter, an investigator at medical school C had been found to use radioactive material on animals without declaring it in his protocol. Moreover, an interviewee on committee C talked about an incident in which the investigator used animals without going through the committee's review.[106] The

investigator submitted a protocol requiring mice for a diabetes study; however, animal staff later found that tumors were growing on several of the mice, which was not part of the study. The investigator then admitted that these mice were actually used in a pilot study of other research that had not been approved.

At university D, the committee is challenged with overseeing the care and use of animals that are maintained in investigators' laboratories instead of the institution's animal facility. Since the animal facility does not meet the requirement of every experiment, some investigators are allowed to maintain animals in their own laboratories. Some investigators also keep animals that have not been approved by the committee. However, the committee makes very few inspections of laboratories; thus, little oversight occurs for these laboratory-maintained animals as well as for experiments conducted in laboratories. An interviewee said, "Theoretically we have to visit every lab to see whether the actual manipulations of animals are in accordance with what they say in the protocols. But we have so many labs at the school that we can't visit them one by one."[107]

The lack of oversight for ongoing projects was not perceived by interviewees in the United States to be a major deficiency of the IACUC system. Only one interviewee at university B talked about the difficulty in overseeing ongoing projects. Since the school conducts little research involving animals, the committee only meets and conducts inspections semi-annually, primarily relying on staff in the animal facility to provide oversight. However, among the four interviewed committees, committee A has developed a relatively effective mechanism in dealing with ongoing projects and

noncompliance issues. Ongoing projects are monitored not only through reports from staff of the animal facilities but also through frequent inspections conducted by a compliance group consisting of both the staff and committee members. One interviewee on the committee said:

> If we look at this protocol and we say or the investigator says, "We're not really sure how this is going to go." Then we say, "Okay, Larry, go and watch this happening and see how it goes." That's pretty common. We do that with some significant percentage of the protocols. And then we do normal follow-ups once a year or so. We go around to every one of the five or six hundreds of protocols that are active. We have someone go to visit the labs and look [at] what's going on.[108]

Because it is difficult to foresee in protocols exactly how an experiment will go, investigators are required to report any deviation or unexpected results in their experiments. However, not every investigator does a good job in self-reporting. When noncompliance is reported by someone other than the investigator, the committee promptly responds by investigating the noncompliance and, if necessary, suspending the experiment. An interviewee from medical school A gave an example:

> Sometimes we get anonymous tips that put into the office, that Professor X is not treating his non-human primate, named Abbot, correctly. So staff immediately investigates and informs the chair, the committee, and depending on preliminary findings, a sub committee may be formed immediately to bring the PI [principal investigator] in, to address these concerns. Sometimes an immediate hold is placed on the protocol and saying, "We don't know what's going on here, but you can't do anymore research on animals until we see through it all." That's rare, but it does happen in times.[109]

The implementation of animal welfare regulations requires not only the review of proposed projects but continuous oversight after approvals are issued. Frequent inspections of ongoing projects and interactions with investigators effectively help ensure

that investigators follow their protocols and comply with regulations. Now that the MGAE system has been established in Taiwan for several years, MGAEs should consider further improving the protocol review system's effectiveness by expanding its education purpose to also include active supervision.

Interactions with Investigators

A number of Taiwanese interviewees felt that the system is resented by investigators. To investigators, the review system wastes their time since it requires them to take an extra step before starting experiments. The system is perceived as simply an obstacle to their research.

Several MGAE interviewees discussed their experiences in communicating with investigators. At medical school C, an interviewee said that her biggest frustration as an MGAE member was investigators being offended by and, thus, purposely disregarding her review comments. She said:

> Now a lot of people who do research . . . hold an opposing attitude [to committee members]. I'm always writing my comments in a polite manner; I would say "Could you consider doing it this way?" Or "Could you provide more information on this?" I always use a polite attitude to communicate with them, like talking to them face to face. And I just provide my opinions. But what happens a lot is that once they get the comments, they immediately feel offended. They think that "You are picking on me." And then they tell you that "I can't make any changes to address your comments." They tell you clearly that it's impossible to modify the experiments. Some of them talk in an uncompromising manner and refuse to explain anything you want them to explain. This situation does happen. . . . They just oppose the committee. Therefore sometimes we need to negotiate with them several times.[110]

At university D, interviewees also face the dilemma of wanting to do a thorough review, while investigators would prefer a quick review. The committee requires

investigators to submit protocols at least two weeks before funding agencies' deadlines of receiving grant applications. However, many investigators typically prepare protocols on the due dates and ask the committee to review and approve their protocols immediately. In these instances, the committee designates one member to conduct an expedited review rather than hold a committee meeting. These investigators also tend to provide insufficient information in protocols; however, the designated reviewers do not have time to send the protocols back and ask for clarifications. "The normal procedure is, you submit a protocol to me, and I take my time reviewing it when I have free time. But now this rarely happens," said an interviewee on committee D. "Now what usually happens is that the guy who works at our animal facility . . . brings the protocol to me and waits here for my review decision. . . . Sometimes I feel really annoyed because he just brings it here and wants the approval right away."[111] "We don't have enough time to do the review. But we don't want to postpone the approval either because otherwise the investigator would be very angry [if he misses the funding deadline]."[112]

The interactions between the Taiwanese committees and investigators indicate that the committees often do not use their authority to require necessary changes in a protocol before it receives approval. Although they are authorized by regulations to decide if an experiment can be conducted, interviewees also care about their relationships with investigators, so they may negotiate with investigators for a middle ground or approve protocols at investigators' requests even though the protocols are still problematic. Investigators do not seem to respect the committees' responsibilities and authorities; instead, they view the review process as merely a bothersome step that

requires extra paperwork. Animal welfare is likely to be compromised by this relationship between the committees and investigators.

Cultural Influences and the Protocol Review Systems

Cultures and social backgrounds of the United States and Taiwan have an influence on the protocol review systems' effectiveness. Protecting animals is generally not promoted by Taiwanese religious or cultural standards. The animal protocol review system is also considered a minor issue by MGAE members. One interviewee said, "Actually our chair thinks that we do this thing [review protocols] because regulations require us to do so. We don't want to affect professors' application of grants. So their application of grants is still the first priority. The system sometimes becomes an impediment."[113] Since few requirements about the review process have been established, MGAEs are inclined to employ the least troublesome review method, which is the designated member review.

The United States has a long history of animal protection with the first anti-cruelty law being enacted in 1828 by New York State's legislators (Leavitt and Halverson 1990). People are generally concerned about the treatment of animals. IACUC members considered protocol reviews to be an important and meaningful process, and they were willing to conduct thorough reviews. One interviewee described how during committee meetings, "Everyone feels obligated to have their input."[114] Although gathering together to review protocols takes a lot of their time, IACUC interviewees were still satisfied with the review process. The interviewee further commented on the review system:

> I like it the way it is. I mean there's discrete amount of time that I know I am going to spend on, probably like between two and five hours in a given week. That's usually over if you count the meetings that spread over a two-week period. So far it's not too onerous as far as I am concerned. . . . This committee can take up an excessive amount of time, and I still feel like I can carry on with other things I have to do. No, it doesn't seem bad, I am relatively happy about how the protocol review process goes.[115]

Reviewing protocols thoroughly and helping investigators comply with animal welfare regulations were considered to be the imperative responsibility of IACUCs by interviewees in the United States. Conversely, in Taiwan, MGAE interviewees were concerned more about their relationships with investigators, who are their colleagues. In Chinese culture, one is generally concerned about how he or she is viewed by other people. Therefore, MGAE interviewees do not want to be harsh to their colleagues. Since only minimum regulatory requirements exist, they may sacrifice the welfare of animals in order to be viewed as a "good person" and maintain good relationships with investigators.

In addition to facilitating the review of the Three R's, establishing protocol review criteria will also improve the MGAE protocol review system's effectiveness by supporting MGAEs' position when investigators disregard their authorities. The lack of regulatory review criteria currently allows investigators to negotiate with MGAEs for approval. Taiwanese people can be so concerned about how they are perceived by others that this can influence decisions that should be based on regulations rather than concern for their own image. This is a cultural influence on MGAE interviewees, which is not as manifested in the culture of IACUC interviewees. One interviewee said, "I think that

current oversight is not good. . . . They [MGAEs] would do their best to approve protocols [by not being critical of minor problems]. The review is not critical."[116]

He further added, "It's because there are no review standards." Clear regulatory review criteria will reduce the prevalence of negotiations between MGAEs and investigators and, thus, will improve MGAEs' oversight of animal welfare.

This consideration of relationship may also make it difficult to supervise ongoing projects in Taiwan. MGAEs may not oversee ongoing projects carefully because they do not want to be strict to their colleagues and friends. Believing that investigators' research should absolutely be respected, one MGAE interviewee said, "This is actually an honor system. We respect him [and believe] that he will follow the protocol."[117]

CONCLUSIONS AND RECOMMENDATIONS

This thesis research finds that both laboratory animal welfare regulations and cultural norms have crucial influences on IACUC and MGAE members' protocol reviews and the protocol review systems' effectiveness in protecting animals. In the United States, during twenty years of implementation, detailed regulatory guidelines and criteria about protocol reviews have been established, and IACUC interviewees employed these guidelines and criteria to assess whether animal welfare is addressed in a protocol. On the other hand, the review system is new in Taiwan, and such review criteria have not been developed. As a result, MGAE interviewees relied on their scientific knowledge to review the scientific design and procedures of a protocol. MGAE interviewees also had lower standards for the treatment of animal pain than IACUC interviewees did. They ignored the importance of monitoring animals to assess their pain and distress and using analgesics to alleviate the discomfort.

The lack of requirements of MGAEs' protocol review process and oversight for ongoing projects also has an impact on the system's effectiveness. Animal protocols in Taiwan can be reviewed by only a few members on a committee without being distributed to all committee members. For ongoing projects, Taiwanese regulations do not require MGAEs to oversee research after approving the protocol. Therefore, interviewees in Taiwan perceived the lack of oversight for ongoing projects to be the major deficiency of the MGAE system.

Since no detailed regulations about the protocol review system exist, culture plays a significant role in the MGAE system's effectiveness in protecting animals. Maintaining

working relationships with investigators is considered more important than protecting animals. Consequently, MGAEs sometimes approve problematic protocols in order to maintain their reputation while maintaining relationships with investigators.

On the other hand, in the United States, compliance with rules and regulations is a top priority. To ensure experiments are conducted in compliance with animal welfare regulations, IACUCs conduct thorough reviews to govern the care and use of animals in research.

This thesis also finds that personal attitudes toward the use of animals in research are less influential on interviewees' protocol reviews. Although interviewees in Taiwan demonstrated diverse and conflicting perspectives toward using animals in research, regulations and cultural norms dominated the reviews of the hypothetical protocols.

The welfare of laboratory animals can be improved in Taiwan by establishing detailed regulations about the protocol review system. Detailed review criteria for addressing the Three R's principle of replacement, reduction, and refinement should be developed to assist the MGAEs' review of animal welfare. Regulations should also require that with designated member review, more than one member should perform the review and additional committee members be given access to the protocol. To ensure research is conducted in accordance with its associated protocol, MGAEs should also conduct follow-up inspections of ongoing research. If a noncompliance is found, MGAEs should be authorized to suspend the research and report it to the COA immediately. Once more detailed regulations are established and enforced, the influence

of cultural norms on the MGAE system can be reduced since MGAEs would then be backed by strong regulatory requirements.

MGAEs' composition of membership should also be further improved by including veterinarians, nonscientists, and nonaffiliated members. Currently, MGAEs in Taiwan do not necessarily contain a veterinarian member; regulations do not require the committees to have nonscientists and nonaffiliated members either. However, interviewees in the United States believed that a diverse membership, including not only scientists but also nonscientists, nonaffiliated members, and veterinarians, is the key to an effective protocol review system.

This thesis research recommends an exchange program between IACUC and MGAE members as well as laboratory animal welfare specialists in the two countries. With the exchange of committee members and animal welfare specialists, MGAEs would benefit from understanding the efficacy of IACUCs' committee composition, protocol review processes, extensive review criteria, and oversight for ongoing projects. This would improve Taiwan's protection of laboratory animals.

To enhance the welfare of laboratory animals in the United States, this thesis research recommends IACUCs strengthen the review of reduction and replacement principles. They should strictly request statistical justifications be provided in protocols. They should also be more critical of the rationale for using animals in each protocol.

The federal Animal Welfare Act should also be amended to match the animal welfare standards required by the PHS Policy. It should require IACUCs to include nonscientist members whose concern is in ethical areas in order to review the care and

use of animals from this perspective. The species covered in the AWA should also be expanded to mice, rats, and birds, which account for approximately 90% of all laboratory animals. Otherwise, no matter how effective the IACUC protocol review system is, the system only governs 10% of laboratory animals under federal requirements.

NOTES

[1] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[2] Member on committee B, interview by author, digital recording, United States, 3 February 2006.
[3] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[4] Member on committee D, interview by author, digital recording, Taiwan, 19 September 2005.
[5] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[6] Member on committee C, interview by author, digital recording, Taiwan, 28 September 2005.
[7] Member on committee D, interview by author, digital recording, Taiwan, 23 September 2005.
[8] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[9] Member on committee A, interview by author, digital recording, United States, 27 February 2006.
[10] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[11] Member on committee A, interview by author, digital recording, United States, 9 March 2006.
[12] Member on committee C, interview by author, digital recording, Taiwan, 29 September 2005.
[13] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[14] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[15] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[16] Member on committee A, interview by author, digital recording, United States, 21 February 2006.
[17] Member on committee B, interview by author, digital recording, United States, 9 February 2006.
[18] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[19] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[20] Member on committee C, interview by author, digital recording, Taiwan, 28 September 2005.
[21] Member on committee D, interview by author, digital recording, Taiwan, 23 September 2005.

[22] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[23] Member on committee A, interview by author, digital recording, United States, 13 February 2006.
[24] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[25] Member on committee B, interview by author, digital recording, United States, 9 February 2006.
[26] Member on committee A, interview by author, digital recording, United States, 21 February 2006.
[27] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[28] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[29] Member on committee D, interview by author, digital recording, Taiwan, 19 September 2005.
[30] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[31] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[32] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[33] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[34] Member on committee B, interview by author, digital recording, United States, 17 February 2006.
[35] Member on committee C, interview by author, digital recording, Taiwan, 29 September 2005.
[36] Member on committee A, interview by author, digital recording, United States, 27 February 2006.
[37] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[38] Member on committee C, interview by author, digital recording, Taiwan, 29 September 2005.
[39] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[40] Member on committee D, interview by author, digital recording, Taiwan, 23 September 2005.
[41] Member on committee C, interview by author, digital recording, Taiwan, 28 September 2005.
[42] Member on committee C, interview by author, digital recording, Taiwan, 14 September 2005.
[43] Member on committee A, interview by author, digital recording, United States, 7 February 2006.

[44] Member on committee B, interview by author, digital recording, United States, 17 February 2006.
[45] Member on committee A, interview by author, digital recording, United States, 9 March 2006.
[46] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[47] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[48] Member on committee B, interview by author, digital recording, United States, 3 February 2006.
[49] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[50] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[51] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[52] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[53] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[54] Member on committee C, interview by author, digital recording, Taiwan, 14 September 2005.
[55] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[56] Member on committee C, interview by author, digital recording, Taiwan, 14 September 2005.
[57] Member on committee C, interview by author, digital recording, Taiwan, 29 September 2005.
[58] Member on committee B, interview by author, digital recording, United States, 17 February 2006.
[59] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[60] Member on committee C, interview by author, digital recording, Taiwan, 27 September 2005.
[61] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[62] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[63] Member on committee A, interview by author, digital recording, United States, 13 February 2006.
[64] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[65] Member on committee B, interview by author, digital recording, United States, 9 February 2006.

[66] Member on committee A, interview by author, digital recording, United States, 9 March 2006.
[67] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[68] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[69] Member on committee C, interview by author, digital recording, Taiwan, 29 September 2005.
[70] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[71] Member on committee D, interview by author, digital recording, Taiwan, 23 September 2005.
[72] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[73] Member on committee B, interview by author, digital recording, United States, 3 February 2006.
[74] Member on committee A, interview by author, digital recording, United States, 27 February 2006.
[75] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[76] Member on committee C, interview by author, digital recording, Taiwan, 27 September 2005.
[77] Member on committee C, interview by author, digital recording, Taiwan, 5 October 2005.
[78] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[79] Member on committee C, interview by author, digital recording, Taiwan, 29 September 2005.
[80] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[81] Member on committee A, interview by author, digital recording, United States, 9 March 2006.
[82] Member on committee A, interview by author, digital recording, United States, 21 February 2006.
[83] Member on committee C, interview by author, digital recording, Taiwan, 14 September 2005.
[84] Member on committee C, interview by author, digital recording, Taiwan, 23 September 2005.
[85] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[86] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[87] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.

[88] Member on committee C, interview by author, digital recording, Taiwan, 14 September 2005.
[89] Member on committee C, interview by author, digital recording, Taiwan, 20 September 2005.
[90] Member on committee C, interview by author, digital recording, Taiwan, 28 September 2005.
[91] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[92] Member on committee A, interview by author, digital recording, United States, 13 February 2006.
[93] Member on committee A, interview by author, digital recording, United States, 7 February 2006.
[94] Member on committee B, interview by author, digital recording, United States, 9 February 2006.
[95] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[96] Member on committee B, interview by author, digital recording, United States, 3 February 2006.
[97] Member on committee A, interview by author, digital recording, United States, 21 February 2006.
[98] Member on committee A, interview by author, digital recording, United States, 27 February 2006.
[99] Member on committee B, interview by author, digital recording, United States, 17 February 2006.
[100] Member on committee D, interview by author, digital recording, Taiwan, 19 September 2005.
[101] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[102] Member on committee B, interview by author, digital recording, United States, 17 February 2006.
[103] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[104] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[105] Member on committee D, interview by author, digital recording, Taiwan, 19 September 2005.
[106] Member on committee C, interview by author, digital recording, Taiwan, 14 September 2005.
[107] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[108] Member on committee A, interview by author, digital recording, United States, 2 March 2006.
[109] Member on committee A, interview by author, digital recording, United States, 21 February 2006.

[110] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[111] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[112] Member on committee D, interview by author, digital recording, Taiwan, 22 September 2005.
[113] Member on committee D, interview by author, digital recording, Taiwan, 20 September 2005.
[114] Member on committee A, interview by author, digital recording, United States, 13 February 2006.
[115] Member on committee A, interview by author, digital recording, United States, 13 February 2006.
[116] Member on committee C, interview by author, digital recording, Taiwan, 21 September 2005.
[117] Member on committee D, interview by author, digital recording, Taiwan, 19 September 2005.

WORKS CITED

Animal Welfare Institute (AWI). 1990. *Animals and Their Legal Rights*, 4th ed. Washington D.C.: Animal Welfare Institute.

Animal Protection Act (APA). 2004. Hua-Zong-(1)-Yi-Tzi-09200248361.

Animal Welfare Act (AWA). U.S. Code. 2002. 7 U.S.C. Secs. 2131-59.

Animal Welfare Regulations (AWRs). Code of Federal Regulations. 2002. 9 C.F.R. Ch. 1.

Bekoff, Marc, and Carron A. Meaney, ed. 1998. *Encyclopedia of Animal Rights and Animal Welfare.* With a forward by Jane Goodall. Westport: Greenwood Press.

Birke, Lynda, and Mike Michael. 1996. Ethics and animal rights extend beyond UK law. Forum for Applied Research and Public Policy (Spring): 35-42.

Blakeley, Donald N. 2003. Listening to the Animals: the Confucian View of Animal Welfare. *Journal of Chinese Philosophy* 30, no. 2: 137-57.

Council of Agriculture (COA). 2003. Regulations for Establishing the Management Group of Animal Experiments. Taipei, Taiwan, R.O.C.

_____. 2004. *實驗動物人道管理九十二年年報* (Humane Management of Laboratory Animals 2003 Annual Report). Taipei, Taiwan, R.O.C.

Dresser, Rebecca. 1989. Developing standards in animal research review. *Journal of American Veterinary Medical Association* 194, no. 9: 1184-91.

Gluck, John P, and F. Barbara Orlans. 1997. Institutional Animal Care and Use Committees: a flawed paradigm or work in progress? Ethics & Behavior 7, no. 4: 329-36.

Houde, Lise, Claude Dumas, and Thérèse Leroux. 2003. Animal Ethics Evaluation: an observational study of Canadian IACUCs. *Ethics & Behavior* 13, no. 4: 333-50.

Ingham, Kim M, Joel A. Goldberg, Hilton J. Klein, Robert G. Johnson, and Michael D. Kastello. 2000. A novel approach for assessing the quality and effectiveness of IACUC oversight in investigator compliance. *Contemporary Topics in Laboratory Animal Science* 39, no. 1: 28-31.

Leavitt, Emily Stewart, and Diane Halverson. 1990. The Evolution of Anti-cruelty Laws

in the United States. In Animal Welfare Institute 1990.

Lee, Mau-Sheng. 2003. 動物權的概念與我國動物保護法的文化意義 (The concept of animal rights and the cultural meanings of our nation's Animal Protection Law). *The Taiwan Law Review* no. 94: 155-80.

Linzey, Andrew. 1998. Christianity. In Bekoff and Meaney, ed. 1998.

National Research Council (NRC). 1996. *Guide for the care and use of laboratory animals.* Washington D.C.: National Academy Press.

Orlans, F. Barbara. 1998. Numbers and Species of Laboratory Animals Used Worldwide. In Bekoff and Meaney, ed. 1998.

Plous, Scott, and Harold Herzog. 2001. Reliability of protocol reviews for animal research. *Science* 293 (Jul): 608-09.

Prentice, Ernest D, David A. Crouse, and Reed W. Ring. 1990. Approaches to increasing the ethical consistency of prior review of animal research. *Investigative Radiology* 25, no. 1: 271-74.

Regan, Tom. 1985. The Radical Egalitarian Case for Animal Rights. In Singer 1985.

Reinhardt, Viktor, and Annie Reinhardt, ed. 2002. *Comfortable Quarters for Laboratory Animals.* Washington, D.C.: Animal Welfare Institute.

Russell, William M.S. 2002. The Ill-effect of Uncomfortable Quarters. In Reinhardt and Reinhardt 2002.

Shih, Shing-Kuang. 2003. 動物保護的本土問題 (Local problems of animal protection work). *Newsletter for Research of Applied Ethics* 26 (Apr): 37-43.

Shih, Chao-Huei. 2005. 動物關懷的理論與實踐–以關懷生命協會的「護生」運動為例 (The theory and practice of animal concerns: Using the "life-protecting" movement of the Life Conservationist Association as an example.) Internet. Available from: http://www.awker.com/hongshi/mag/78/78-7.htm; accessed 10 October 2006.

Singer, Peter, ed. 1985. *In Defense of Animals.* Oxford: Basil Blackwell.

Singer, Peter. 1990. *Animal Liberation*, 2d ed. New York: The New York Review of Books.

Stafford, Jennifer M, Larry W. Brewer, and James A. Gessaman. 2003. Avian food selection with application to pesticide risk assessment: are dead and desiccated insects a desirable food source? *Environmental Toxicology and Chemistry* 22, no. 6: 1335-39.

Steneck, Nicholas H. 1997. Role of the Institutional Animal Care and Use Committee in monitoring research. *Ethics & Behavior* 7, no. 2: 173-84.

U.S. Department of Health and Human Services (USDHHS), National Institutes of Health, Office of Laboratory Animal Welfare. 2002a. *Institutional Animal Care and Use Committee Guidebook*, 2d ed. Washington, D.C.

_____. 2002b. Public Health Service Policy on Humane Care and Use of Laboratory Animals. 67 Federal Register 51289.

U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service, Animal Care. 2004. *FY 2004 AWA Inspections*. Internet. Available from http://www.aphis.usda.gov/ac/awreports/awreport2004.pdf; accessed 4 September 2006.

U.S. Office of Science and Technology Policy (USOSTP). 1985. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training. 50 Federal Register 20864.

Wemelsfelder, Francoise. 1998. Animal Boredom. In Bekoff and Meaney, ed. 1998.

Wong, Yuk. 1979. Attitude of Chinese religions and Christianity towards the animal kingdom. *Journal of Dharma* 4, no. 1: 47-55.

Yeh, Lih-Sen. 1995. *動物與法律* (Animal and Law). Taipei: Animal Protection Association of the Republic of China.

Zurlo, Joanne, and Alan M. Goldberg. 1998. Reduction, Refinement, and Replacement (the Three Rs). In Bekoff and Meaney, ed. 1998.

Zurlo, Joanne, Deborah Rudacille, and Alan M. Goldberg. 1994. Animal and Alternatives in Testing: History, Science, and Ethics. Internet. Available from http://caat.jhsph.edu/publications/animal_alternatives/chapter5.htm; accessed 15 March 2005.

APPENDICES

A. IACUC and MGAE Interview Questions

I. General Information

1. What is the position that you hold right now?
2. How long have you held this position?
3. What is your area of expertise?
4. Have you ever participated in research or teaching involving animals? Do you use animals now? What species do you use?
5. Where did you get your degrees and in what did you get them?
6. How long have you served on the IACUC?
7. What was the reason that made you become a member of the IACUC?
8. What species of animals does your school use?
9. How many protocols do you review annually?
10. How much time do you spend reviewing a protocol?
11. What references/guidelines do you use to review a protocol?
12. What IACUC member training have you ever had?

II. Protocol Review Process

13. What is the protocol review process in your school for a standard submission?
14. When you review a protocol, what are the three aspects of the protocol that you consider most important? What are your reasons for choosing them?
15. What are your standards for these aspects?

16. Under what circumstances will you recommend to disapprove a protocol?
17. What is generally your biggest frustration when reviewing protocols?
18. In your opinion, what is effective about the protocol review system in your school?
19. What are the shortcomings in the protocol review system?
20. What are your recommendations to improve the effectiveness of protocol reviews in your school?

III. Hypothetical Protocol Reviews

21. Here are two protocols. Please review them following the methods and standards that you often use. What are your gut-feelings about protocol A/B?
22. What is your decision about protocol A/B? Would you recommend approval for protocol A/B?
23. How does the amount of information provided in this protocol differ from your school's submissions?
24. In your opinion, how is the scientific value of protocol A/B?
25. What is your opinion about the experimental design?
26. What is your view about the selection of animal model?
27. What is your attitude concerning the numbers of animals used?
28. (For the parabiotic mice protocol only) What degree of pain and distress will the research cause to the animals? Please rate from 1-10. (10 is most painful.)
29. What is your opinion regarding the measures used to reduce animal pain and distress?
30. Is there anything else you want to ask/say about the protocols?

IV. Personal Information and Attitudes

31. Would you mind telling me your age? Or, would you mind telling me what 10-year range you are in?
32. Have you ever studied or live abroad? Could you tell me where?
33. Do you have religious beliefs?
34. Some people think that animals hold an equal status to human beings, which means animals have rights to live, and people have no rights to experiment on them. What is your opinion about that?
35. Have you ever have pets?
36. Do you belong to, or ever donate money to/support any animal welfare organizations?

B. Parabiotic Mice Protocol

PROTOCOL FOR ANIMAL CARE AND USE

Submit hardcopies of all proposals to the Office of Sponsored Projects, Bldg MT.
For questions or submissions, contact the OSP administrator at extension 6-2121. OSP #: _____

Principal Investigator: Dr. Joseph Keller **Contact #:** 586-0911

Affiliation: Faculty

Department: Dept. of Medicine, Division of Immunology

Project Title: Distribution of IgG and IgM in the mouse parabiotic model

Research location: R-132

Funding Source: NIH

Proposed Study Period October 1, 2006 *to* November 30, 2006

A. Animal Specifications:

	Species name	Strain	Numbers to be used	Source	Housing location
1.	*Mus musculus*	Swiss Webster-Female	30	Charles River	ACF
2.	*Mus musculus*	SW/Lf2-Female	30	Charles River	ACF

1) **Specify if any species listed are considered endangered or a threatened:**

NONE

2) **Do you have the appropriate government permit to acquire or hold these species?**

N/A

3) **For wild caught animals, describe method of capture, capture site and quarantine procedures:**

N/A

B. Personnel Working with Animals:

Name	Affiliation	Involvement Period	Relevant animal handling experience/Certification
1. J. Keller	Faculty	2 months	13 years experience with rodent anesthesia/surgery
2. Linda Liu	Grad student	2 months	5 years experience with rodent anesthesia/surgery

C. Animal Housing and Care:

(Detail procedures for routine housing and veterinary care if other than the institution's Animal Care Facility standard operating procedures. Describe personnel responsible for direct animal care of each species, relevant experience and training)

There will be standard housing conditions and a 7-day acclimation for all mice prior surgery. Post surgery, animals will be maintained on absorbent paper until wounds heal (approximately 5-7 days) and shall have 2.4gm of trimethoprim sulfa (antibiotic) oral suspension placed into the drinking water for 7 days. Moistened rodent chow and a crock of water shall be provided on the cage floor to encourage normal fluid and food intake.

D. Rationale for Using Animals:

(Use lay terms to describe purpose of the research and the appropriateness of the numbers of animals to be used)

The purpose of this study is to assess the dynamics of passive immunity in the parabiotic mouse model. Little is known about the effects of passive immunity shared between parabiotic pairs for studies of congenital disorders (such as diabetes and leukodystrophies) affected by immune and metabolic function (Partridge, T.A. et al 2002). Specifically, little is known about the migration and infiltration of immuno-globulins between parabiotic mouse pairs. Due to limitations of current systems, it is difficult to ascertain the migration patterns of immunoglobulins *in vivo*. Our approach will be to join an inbred strain (mouse A) with a mouse of a similar background whose phenotype has a protein marker embedded on the globulin chain, SW/Lf2

(mouse B). Through serological testing and tissue harvesting we will be able to quantify the degree of passive immunity between the parabiotic pairs at specific time points in blood and tissues.

Much is known about the immunological status of Swiss Webster mice (Conboy, I.M., Conboy, M.J., Smythe, G.M. & Rando, T.A. *1994*). For statistically significant results, we have determined that a minimum of 25 parabiotic pairs of mice should be evaluated for distribution of immunoglobulins. Successful parabiotic union is essential for this study and we will request an additional 10 animals as replacement subjects to insure we have all necessary pairs for this work. Hence, the total number of animals requested for this study is 60 mice.

E. Experimental Use of Animals:
(Describe all methods and procedures in lay terms)

1. Methods and Procedures:

Mice (SW and SW/Lf2, female, 2 months of age) will be allowed 7 days to acclimate from arrival to the Animal Care Facility. A pre-immune blood sample will be obtained from orbital sinus plexus (0.1 – 0.2mL) under general anesthetic (pentobarbital) from each mouse. Once surgery is performed, the animals will be allowed to recover on absorbent paper and monitored closely by research personnel. Once fully recovered, subsequent blood samples (0.1-0.2mL) will be taken solely from mouse A on days 7, 14, 28, 36 and 48 post-surgery.

2. Experimental drugs:
(include dose, volume, route and frequency of administration)

N/A

3. Anesthetic, Sedative, Tranquilizing or Immobilizing agents:

Sodium pentobarbital will be administered at around 40mg/kg intraperitoneally for surgical procedure. To immobilize the mice for subsequent routine blood collection, Isoflurane anesthesia will be delivered by precision vaporizer into an induction chamber until effect.

4. Surgery and Perioperative care:

The animals will be surgically prepared by shaving the hair followed by application of a topical antiseptic (betadine). An incision will be made on the left lateral aspect of the mouse A and on the reciprocating side of mouse B (refer to diagram 1). The incision will start from skin at the base of the ear and extend to the base of the tail. The lateral muscle wall of each mouse extending from hind edge of the last rib to just infront of the ilium will be severed and all subsequent bleeding controlled. The surgeon will then close the open area by suturing the mice together (4-0 silk ties). The ventral skin flaps and the abdominal muscles will be closed first using silk suture. The surgeon will then use non-absorbable monofilament suture join the scapulae together in a mattress pattern. The lilac bones will also be joined together using this technique. Finally the opposing skin edges will be united using absorbent suture under the skin. A topical triple antibiotic ointment shall be applied to the incision area immediately upon recovery. Total surgery time is approximately 40 minutes.

5. Analgesics and Supportive care:

Burprenorphine will be administered to each mouse at 0.05mg/kg SQ once the animals begin to show signs of ambulation and every 8-12 hours thereafter as needed for discomfort by laboratory personnel. To facilitate their initial recovery, moistened rodent chow and a heated water blanket will be made available to the mice. Mice tend to fair better as a parabiotic union than other recorded species and little to no complications are expected.

Animals will be monitored closely for appetite and lethargy throughout the study.

5. Restraint procedures
(provide monitoring details of animals restrained for >4 hrs)

There will be no manual or chemical restraint greater than 4 hours for this study.

F. Study Endpoint:
(Include method of euthanasia and final disposition of animals and tissues)

On day 48 post-surgery, parabiotic pairs will be introduced to slow rate of carbon dioxide gas and euthanized by asphyxiation. 0.5mL of whole blood will be obtained from both mice (post-mortem) by cardiac puncture using a tuberculin syringe and 25ga needle to measure IgM levels at day 48. A gross necropsy examination will be performed on both mice to gauge the extent of post-surgical adhesion, while lymph tissue (thymus and nodes), gut, and striated muscle samples will be taken to analyze for IgG levels in the tissues. Animal carcasses will then be put in biohazard bags and placed in the Animal Care Facility cold room.

G. Hazardous Materials:

1. Check all that apply: □ Biohazard (Infectious or carcinogenic)
□ Chemical Hazard (Toxic) □ Radioisotope □ Other:

None.

3. Location, handling, protective gear and disposal procedures:

N/A

4. Personnel to handle hazardous material:

N/A

5. Safety board review and necessary permits:

N/A

H. Signature of Principal Investigator:

I certify that all information herein is true and accurate, and that I shall abide by all government and institutional policies with regard to animal care and use.

Name	Signature	Date

I. IACUC approving signature:

Name/Title	Signature	Date

J. Reviewer comments:

C. Wild Bird Protocol

PROTOCOL FOR ANIMAL CARE AND USE

Submit hardcopies of all proposals to the Office of Sponsored Projects, Bldg MT.
For questions or submissions, contact the OSP administrator at extension 6-2121. OSP #: _____

Principal Investigator: Dr. Yulan Carr **Contact #:** 252-6179

Affiliation: Faculty

Department: Biological Sciences

Project Title: ASSESSMENT OF AVIAN FOOD SELECTION AND THEIR RISK TO PESTICIDE

Research Location: Animal Care Facility

Funding Source: EPA

Proposed Study Period Feb 2006 *to* Jul 2006

A. Animal Specifications:

Species name	Strain	Numbers to be used	Source	Housing location
1. Common Starling (*Sturnus vulgaris*)		100	wild caught	ACF
2. N/A				

1) **Specify if any species listed are considered endangered or threatened:**

None.

2) **Do you have the appropriate governmental permit to acquire or hold these species?**

N/A

3) **For wild caught animals, describe capture site and quarantine procedures:**

The birds will be captured from state parks and open spaces by means of baited walk-in funnel traps. After getting caught, each bird will be sent to an aviary of the Biological Sciences Department for quarantine. The birds

will stay at the aviary until 100 birds have been captured and quarantined for at least 5 days.

B. Personnel Working with Animals:

Name	Affiliation	Involvement Period	Relevant animal handling experience/Certification
1. Yulan Carr	Faculty	4-6 months	14 yrs experience in avian toxicology
2. Jason Wu	Grad Student	4-6 months	3 yrs experience in avian toxicology
3. Nancy Williams	DVM	4-6 months	8 yrs experience in avian medicine

C. Animal Housing and Care:

(Detail procedures for routine housing and veterinary care if other than the institution's Animal Care Facility standard operating procedures. Describe personnel responsible for direct animal care of each species, relevant experience and training)

The animals will be quarantined in an aviary of the Biological Sciences Department for 5 days prior to the research. After quarantine they will be sent to the school's Animal Care Facility and placed in individual cages. Each bird will be housed in a 30.5 cm x 30.5 cm cage. Solid dividers will be placed between cages to avoid any possible aggressive behavior. Temperature will be maintained at 18 to 24°C, and lights will be kept at 12:12hr light:dark period. The animals will be provided with dry wild bird food and water. There will be a 24-hour acclimation for the animals prior to the experiment.

D. Rationale for Using Animals:

(Describe purpose of the research and the appropriateness of the numbers of animals to be used)

The purpose of the study is to assess the risk of pesticide exposure to avian species through dietary, which has known to be the major pathway of pesticides to wildlife. Most invertebrates die immediately after the

application of pesticides; however, whether birds consume chemical-killed insects is still unknown. This study aims to investigate wild, adult birds' food selection between live and dead invertebrates. The common starling is chosen for the study because of its non-native status, abundance throughout North America, and omnivorous foraging behavior. It also serves as a surrogate that helps us understand pesticide risks to other rare avian species. In order to obtain statistically significant results, one hundred common starlings will be captured from the wild and used in this research.

E. Experimental Use of Animals:

1. Methods and Procedures:

Every four days, the animals will be provided with live crickets, pesticide-killed crickets, and crickets frozen to death. Wild bird food will be withdrawn during experimental days. Total experimental period is 90 days.

2. Experimental drugs:
(include dose, volume, route and frequency of administration)

No drugs will be applied directly to the animals. Chlorpyrifos, an insecticide widely used on farms as well as in homes, will be employed to create pesticide-killed crickets.

3. Anesthetic, Sedative, Tranquilizing or Immobilizing agents:

N/A

4. Surgery and Perioperative care:

N/A

5. Analgesics and Supportive care:

N/A

6. Restraint procedures:
(provide monitoring details of animals restrained for greater than 4 hours)

N/A

F. Study Endpoint:
(Include method of euthanasia and final disposition of animals and tissues)

This study requires three months to complete. After 90 days of experiment, the animals will be euthanized with sodium pentobarbital. The investigator will dissect the animal to examine the pesticide content in the livers. Animal carcasses will be put in biohazard bags and placed in the cold room depository.

G. Hazardous Materials:

1. Check all that apply: □ Biohazard (Infectious or carcinogenic)
× Chemical Hazard (Toxic) □ Radioisotope □ Other:

2. Location, handling, protective gear and disposal procedures:

This research will take place at the school's Animal Care Facility. All personnel will be wearing masks, lab coats and gloves when handling chlorpyrifos.

3. Personnel to handle hazardous material:

Dr. Carr and her assistant, Mr. Wu and Dr. Williams, will be handling chlorpyrifos.

4. Safety board review and necessary permits:

N/A

H. Signature of Principal Investigator:

I certify that all information herein is true and accurate, and that I shall abide by all governmental and institutional policies with regard to animal care and use.

_____

Name Signature Date

I. IACUC approving signature

Name/Title Signature Date

J. Reviewer comments: